

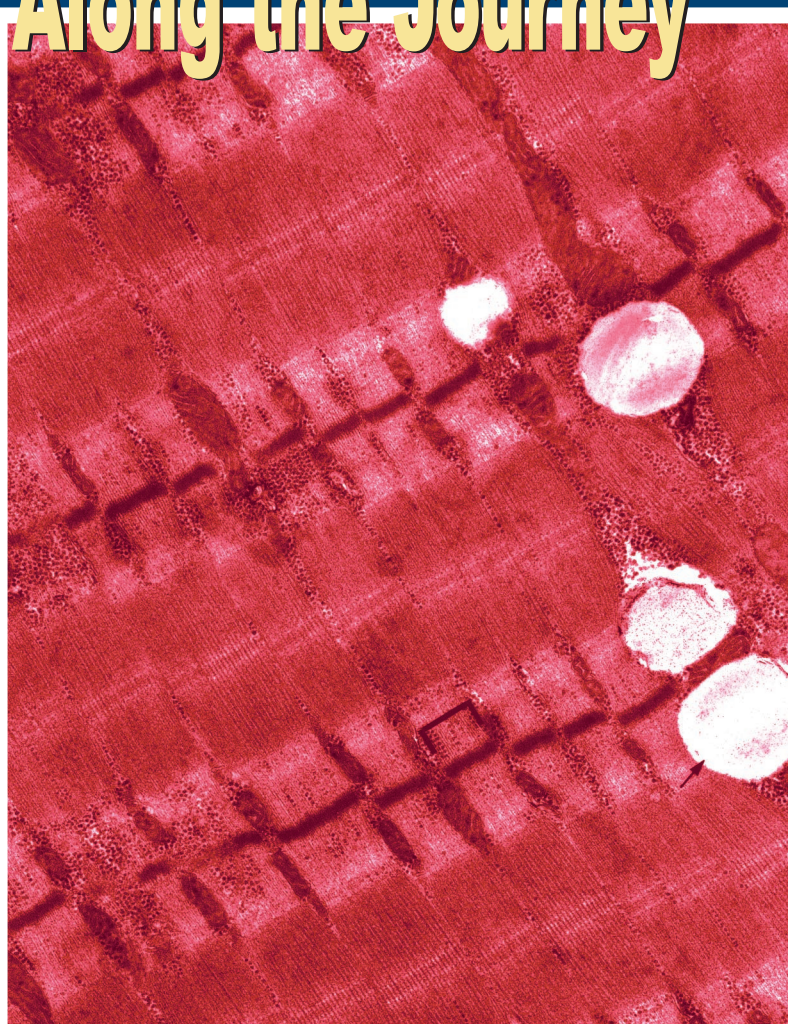
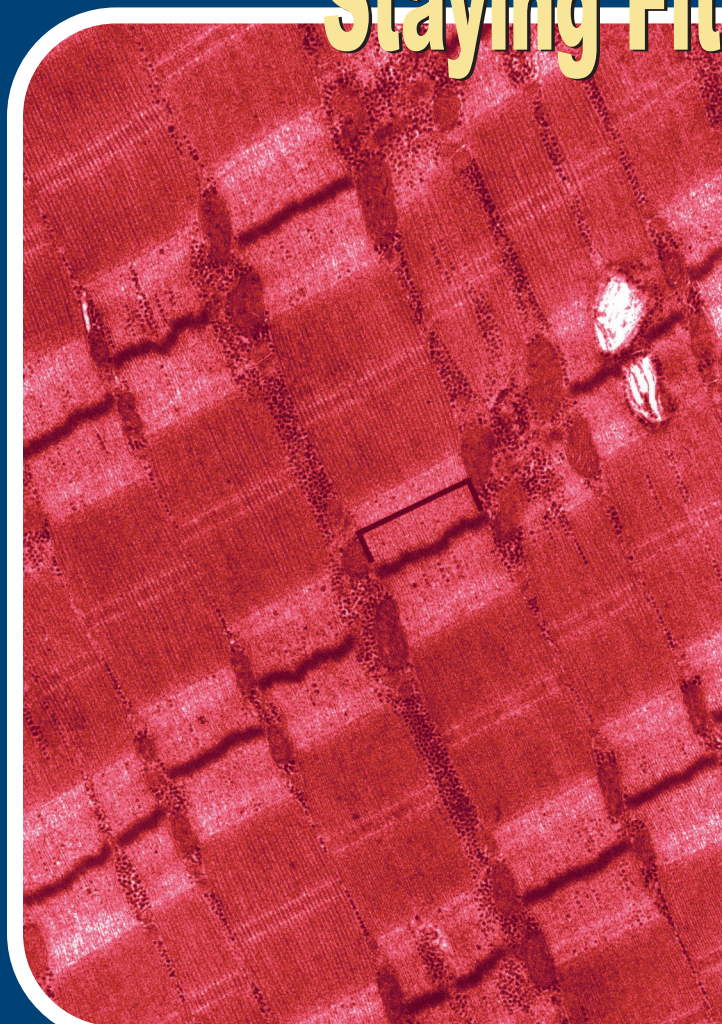
Reproduction in Space • Casting Technology • Dusty Plasmas • Orthostatic Intolerance in Astronauts

Space Research

Office of Biological and Physical Research

March 2002, Vol. 1 No. 2

Staying Fit Along the Journey



Profile:
Alice
Gast

National Aeronautics and
Space Administration

Letter From the Associate Administrator



NASA's Office of Biological and Physical Research's (OBPR's) mission is to use the synergy among physical, chemical, and biological research in space to acquire fundamental knowledge and to generate applications of that knowledge for space travel and on Earth. Our goals as NASA's fifth and newest enterprise are to conduct research for safe and productive human habitation in space; to use the space environment as a laboratory for testing fundamental principles of physics, chemistry, and biology; to enable and promote commercial research in space; and to use space research opportunities to improve academic achievement and quality of life on Earth. With the advent of the International Space Station (ISS), and its continuously operating microgravity environment, we take a major step toward meeting our goals.

Our feature story, Human Physiology Research and the ISS, highlights biotechnology and biomedical research on the ISS. This orbiting laboratory will be in the spotlight in three areas: research in physiological effects of space travel and in countermeasures to those effects; research in other disciplines to advance scientific understanding; and applications of the above research to improving life on Earth. OBPR will be the key player in ISS research in the coming months and years.

As we move from short-duration space shuttle missions of a few days to extended-duration missions on the ISS, we must be acutely aware of and must counter the negative effects of spaceflight on the ISS crew. OBPR research ensures a safe and healthy crew during their stint in space and upon their return to Earth. OBPR research and technologies will also develop the capabilities for extended-duration missions that will ultimately point the way beyond low Earth orbit to space missions lasting months, even years. It is not a question of if, but when. And when that time comes, NASA will make sure the spacefaring crew can venture safely to those far regions in space.

In addition to the role of the ISS as a place for physiological research, the station serves as a continuous microgravity laboratory where iterative science can be conducted to test probing hypotheses and lines of inquiry that will advance the generation of new knowledge. For example, we will be able to examine the results of multigenerational microgravity growth of plants and other living organisms — as the capability of the ISS evolves, we look forward to advances in a number of fundamental fields of science. We will be able to peer into the realm of physical systems not reachable on Earth like macroscopic quantum systems.

Third, research conducted in space will result in advances here on Earth as illustrated by the phrase we use, "Space Research and You." Insights gained through fundamental science, research on humans living and working in space, and commercial research conducted in space will greatly benefit medical research on Earth. Lessons learned to enable the crew to sustain bone growth and muscle strength and to minimize balance disorders may directly aid people on Earth suffering similar maladies as a result of injury, disease, or the natural aging process. We have forged partnerships with the Juvenile Diabetes Foundation, the National Institutes of Health, and other fine agencies and organizations to advance the fields of disease diagnosis and treatment, including the use of telemedicine, which extends medical care to remote locations, be it the ISS or a remote region on Earth.

In fact, our research in biotechnology on the ISS has taken on added dimensions since the terrorist attacks of last September and the use of anthrax as a tool of bioterrorism. The ISS, as a unique closed-environment laboratory, maintains a rigorous system of air and water filtration and environmental monitoring that can also aid those charged with system safety on Earth. For example, the Electronic Nose (E-Nose) uses polymers to detect different classes of compounds as an early warning system for chemical hazard events. The same technology can be adapted for use on Earth for chemical detection in buildings and other closed systems. Technology developed for bacteria detection systems on the ISS to ensure safe food and a safe drinking water supply for astronauts can be used to assess municipal water supplies on Earth. In short, the advances in sustaining a healthy crew environment within the sealed habitat of the ISS in space have direct application and benefit to those charged with maintaining healthy standards of our basic resources on Earth.

Of course, there is yet another contribution the International Space Station can make. In a world beset by turmoil and conflict, the path of the station peacefully crosses many national boundaries. The ISS is a product of multinational efforts in its development. Also, the ISS crew reflects an international profile of spacefarers, with other nations likely to see their country represented in the faces of future crewmembers. As ISS commander Frank Culberston so poignantly noted last fall, the ISS can serve as a role model for international collaboration and cooperation.

A handwritten signature in black ink that reads "Kathie L. Olsen". The signature is fluid and cursive, with the first name being the most prominent.

Kathie L. Olsen
Acting Associate Administrator
Office of Biological and Physical Research

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On the cover:

Two sections of muscle fiber obtained from an astronaut before (left) and after (right) spaceflight illustrate the atrophy that occurs over time in a microgravity environment. The muscle section on the right has thinner myofibrils (a functional unit of muscle) and white lipid droplets, which indicate decreased functionality, or atrophy. This electron microscope image has been tinted for design purposes.

credit: Dan Riley, The Medical College of Wisconsin

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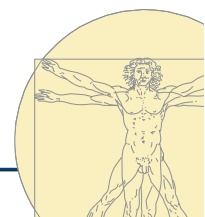
Alice Gast envisions a future for science in which disciplines have flexible borders and researchers collaborate across those borders.

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In the Spirit of Cooperation



credit: Donna Covey

Recipients of the Prince of Asturias Award receive 5 million pesetas (just over \$27,000), a sculpture (shown here) designed by the late Spanish artist Joan Miró especially for this award, a diploma, and an insignia.

The International Space Station (ISS) joined a list of famous previous recipients, including Nelson Mandela and Frederick W. DeKlerk, and Mikhail Gorbachev, among others, when it received the 2001 Prince of Asturias Award for International Cooperation.

The Prince of Asturias Awards, first granted in 1991, promote and reward scientific, technical, cultural, social, and humanistic work by individuals or groups throughout the world. The award for international cooperation is granted to the "individual, group, or institution from any country in the world who, by transcending national frontiers, has contributed in an exemplary manner to mutual understanding, progress, and brotherhood between nations."

His Royal Highness the Prince of Asturias, Felipe de Borbón of Spain, presented the award on October 26, 2001, in Oviedo, Spain, to representatives of the Canadian Space Agency, the European Space Agency, NASA, the National Space Development Agency of Japan, and the Russian Aviation and Space Agency. Prince Felipe also placed a congratulatory call to the Expedition 3 crew and the *Soyuz 3*

transport crew, who were aboard the ISS at the time.

The ISS was nominated for the award by the Spanish Center for Space Law because the station's purpose and construction have greatly contributed to developing and sustaining international cooperation, thereby meeting the spirit of the 1967 Treaty on Principles Governing the Activities of States in the Exploration and Use of Outer Space, Including the Moon and Other Celestial Bodies, which espoused exploring space for the benefit of all humans and called for international cooperation on all scientific research.

Construction of the ISS, which orbits 250 miles above Earth, began in 1998, and crews of three have been living and working onboard for four-month stints since November 2000. Several research efforts have already taken place on the ISS, with plans for a number of science disciplines to use the unique, continuous microgravity environment for biological, physical, technological, and commercial space research.

Optimizing OBPR Resources

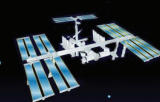
To optimize funding and research resources, the Office of Biological and Physical Research (OBPR) has assembled an *ad hoc* task force for Research Maximization and Prioritization (REMAP). The task force is charged with identifying high-priority science and technology problems to be addressed by OBPR-funded research and with defining the evaluation criteria that will enable OBPR to create a prioritized road map and implementation timetable for the period from 2003 to 2020.

NASA Administrator Sean O'Keefe appointed the members of the task force, which includes leading scientists and technologists from academia, government, and industry with expertise spanning relevant disciplines in the biological and physical sciences. Most members are individuals who are not involved with NASA programs, which provides a nonagency perspective to the proceedings. The committee chair is a nationally recognized leader in science and technology research or a valued contributor to science and technology policy. Members were appointed as special government employees.

The first of a series of three meetings of the REMAP task force took place in early spring. A final report and a draft of prioritized OBPR programs are due in late spring 2002, and will be presented to the NASA Advisory Council (NAC), which will consider the report and formally present its recommendations to the NASA administrator for an agency response. OBPR will use this report to help develop research priorities and the research road map between June and August 2002 and will present the road map to the National Academy of Sciences, the Office of Science and Technology Policy, and the Office of Management and Budget (OMB) in August 2002. The NASA chief scientist's office will use the REMAP task force report to lead the integration of all NASA International Space Station activities, and will report back to NAC in September. The derived research priorities will be reflected in the fiscal year 2004 NASA budget that will be finalized with the OMB.

For more information on OBPR REMAP activities, contact Mark C. Lee, Task Force Executive Secretary, at NASA headquarters: mlee@hq.nasa.gov.

ISS: Coming to a Sky Near You...



NASA now has two web sites for people interested in seeing satellites, the International Space Station (ISS), or the space shuttle (when in orbit): one from Marshall Space Flight Center (<http://liftoff.msfc.nasa.gov/toc.asp?s=Tracking>) and one from Johnson Space Center (<http://spaceflight.nasa.gov/realdata/sightings/>).

The Marshall site, Liftoff, leads to pages showing where the ISS and various satellites are in real time, including altitude, longitude, and latitude. Site visitors can also follow the spacecrafts' trajectories across the globe. Another Liftoff page, located at <http://liftoff.msfc.nasa.gov/RealTime/Jpass/20/>, allows visitors to enter their zip code (or latitude and longitude) to display tracks of the ISS, satellites, or the

shuttle relative to their location. The site lists all the passes over the selected location during a 24-hour period and can display sky charts of the passes as they look to observers on the ground.

The Johnson site, NASA SkyWatch, is also a guide to seeing orbital vehicles in the sky. Visitors can simply type in their city to see what will be flying overhead in the next two weeks. NASA SkyWatch also has a short informational video and tips for successful sightings. In addition, it has a Quick Start Guide showing stars, constellations, the Sun, the Moon, and visible planets as well as the path of the orbital vehicle to make tracking easier.

View the International Space Station From Your Backyard!



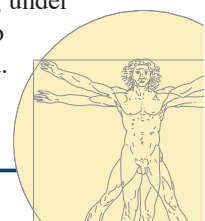
Eighth-grade winners of an essay competition from Walter R. Sundling School in Palatine, Illinois, helped to load macromolecular crystal growth samples for transport to the International Space Station aboard STS-110. By involving students in his research, Principal Investigator Alexander McPherson, of the University of California, Irvine, has encouraged their interest in biology and space research. Here, Merle Myers, of Marshall Space Flight Center, demonstrates the loading process to several of the competition winners.

Goldin Instrumental in Formation of OBPR

On November 17, 2001, NASA Administrator Daniel Goldin retired after nearly 10 years of service at the helm of the U.S. space agency. During his tenure, the International Space Station became a reality, and a new enterprise, the Office of Biological and Physical Research (OBPR), was formed to take advantage of the space environment as a tool to advance research in the fields of biomedicine and biotechnology.

The 19th century was characterized as the Industrial Revolution. The latter part of the 20th century, with its dramatic computational and communication advances, became the Information Revolution. With the new millennium, we are at the threshold of yet another revolution: the Biology Revolution. It is a time of rapid advances in the development of new drugs; research on DNA; research on stem cells that may lead to organ replacement capabilities; improvements in disease prediction, early detection, and treatment; and other biotechnological and biomedical breakthroughs yet to come. Some research has raised questions of ethical issues, requiring dialogue on what should and should not be attempted. The recognition of the role biotechnology would play in the coming century and the role that microgravity research could play within the fields of biotechnology and biomedicine prompted the creation of the new enterprise.

The new enterprise was further validated when Congress and the new presidential administration doubled the OBPR budget in the fiscal year 2002 appropriations bill. With the additional funding, scientists working under the auspices of the enterprise will have even greater opportunity to carry out their groundbreaking work for the benefit of humankind.



Human Physiology Research Staying Fit Along the Journey

The human body undergoes numerous adaptations when it leaves Earth's gravity. Researchers are studying how to minimize those physiological changes in astronauts and in people on Earth with similar health conditions.

Imagine the sensations of being an astronaut — the force of rocket thrust pushing you skyward while Earth's gravity struggles to keep you in its grip; the view from the cockpit as you climb higher and higher; and finally, many minutes later, when the space shuttle has reached its orbit and is in freefall around Earth, the giddy freedom of “floating” through air as you “swim” from spot to spot, tumbling in a slow-motion somersault now and then, just because you can.

But there's more. Now imagine the cold-like sinus and nasal stuffiness you get as fluids shift upward in your body, no longer pulled to your feet by gravity. Though you would not be able to feel it, there is a gradual

weakening of your heart and other muscles since they are no longer challenged to resist the pull of gravity. Similarly, there is bone loss as your limbs no longer have to bear the skeletal weight they do every day on Earth. These are a few of the adaptations the body makes when an astronaut travels on the International Space Station (ISS) or on any other orbiting spacecraft.

All these adjustments can make work in space more difficult, and they definitely pose problems when an astronaut re-enters Earth's gravity at the end of a mission. Upon returning to Earth, the muscles and bones weakened in space need to readjust to gravity's pull, and fluids that have shifted and been expelled by the

body need to be replaced. To minimize the physiological effects of long-term travel in space, scientists supported by NASA's Office of Biological and Physical Research (OBPR) are conducting research on humans, on other life forms, and even on individual cells. As they find the causes of the physiological effects and devise countermeasures to minimize their impact, scientists are also learning more about how to combat similar health conditions that occur on Earth.

Getting a Workout in Space

Good old-fashioned exercise can reduce some of the physiological deficiencies associated with spaceflight, and getting the right exercise prescription is just what Donald Hagan, exercise lead for the Human Adaptation and Countermeasures Office and director of the Exercise Physiology Laboratory at Johnson Space Center, is looking for. Exercise prescriptions are the individualized exercise plans that astronauts follow to maintain their aerobic capacity, bone density, and muscle mass as much as possible during flight. Hagan's group works with the astronauts themselves, recommending preflight fitness plans, training the astronauts for in-flight use of the exercise equipment onboard the ISS, and monitoring the health of astronauts after their return to Earth.

The researcher's studies are related to three different exercise machines, the leg cycle ergometer, the treadmill, and the interim resistance exercise device. The cycle ergometer was the first exercise device to be flown on spacecraft; it flew on *Skylab* and Russian Space Station *Mir*, and is now on the ISS. Astronauts can use this versatile piece of exercise equipment to cycle with their legs or their arms to gain aerobic conditioning benefits. Before flight, astronauts complete a baseline test on the equipment to determine their maximum workload.

During flight, all astronauts are required to complete physical fitness tests on the equipment once a month. The workloads for the test are based on the subject's maximum workload capacity determined before flight. Hagan describes the test protocol: “They have 5 minutes of rest, 5 minutes at 25 percent, 5 minutes at 50 percent, 5 minutes at 75 percent of their



credit: NASA

Exercising in space on a cycle ergometer and other suitable equipment can go a long way toward lessening such conditions as muscle atrophy and bone loss, which occur in microgravity.

capacity, and then they do a 5-minute recovery at a low workload. Each crewmember has his or her own workload protocol.”

The purposes of the test are to determine the relationship between the heart rate and the power output, and to see how much the relationship has changed compared to the preflight test. The goal is for the in-flight relationship to be the same as the preflight relationship.

Hagan illustrates, “For example, let’s say that on the ground their heart rate at the 25-percent workload is 110 beats a minute, at 50 percent workload it’s 140 beats a minute, and at the 75 percent workload, let’s say up to 160.

“Next we take them into flight and we do the same test. At 25 percent, instead of being 110, the heart rate is now 115. Then at 50 percent workload, instead of being 140 it’s 150, and at the 75 percent workload, instead of being 160, it’s 175. So what that tells us is that for any given workload they have a higher heart rate and a decrease in their aerobic capacity.

“When we see that, we’ll write an exercise prescription or change their current exercise prescription in-flight to increase their actual aerobic conditioning and training, so that we can bring that relationship back in line with what it was during preflight.”

The second device used in the exercise plans is the treadmill, which is operated in both motor-driven and self-driven modes. Hagan describes, “The astronaut is held to the treadmill surface using a subject-loading device that consists of two spring-loaded cords that come up from either side of the treadmill and are attached to a harness that fits around the waist of the astronaut. The cords holding the astronaut to the treadmill can be loaded with anywhere from 66 percent to 100 percent of the subject’s body weight.” Optimum loading is usually about 75 percent of the astronaut’s weight on Earth.

According to Hagan, treadmill exercise stresses multiple systems. It not only allows for sustained, rhythmic exercise for 20 to 30 minutes, so astronauts can simulate walking and running on Earth, but it also can be loaded to levels that provide more resistance during a workout. “That added resistance should help to maintain bone density and muscle mass that is so easily lost during spaceflight,” explains Hagan.

The third exercise machine is the interim resistance exercise device, or IRED. Hagan describes the equipment: “The IRED is basically two cylinders, and inside each of these cylinders are 13 disks, or flex packs. The flex packs are connected to a central axle with a series of rubber connections.”

The astronaut sets the number of flex packs to be engaged and pulls on a cord tied to the axle. The flex packs create resistance; the greater the number of flex packs, the greater the resistance, up to 300 pounds per cylinder.

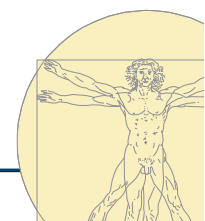
The weight-lifting or strength device also can be used for other exercises. “We have a shoulder harness system [that can be attached to the IRED] so astronauts can do deep knee bends, what we call squats,” says Hagan. “They can do back exercises, they can do heel raises. Basically, they’re taxing what we call the antigravity muscles: the calves, the thighs, the buttocks, all the back muscles — all those muscles that are engaged when you stand up.”

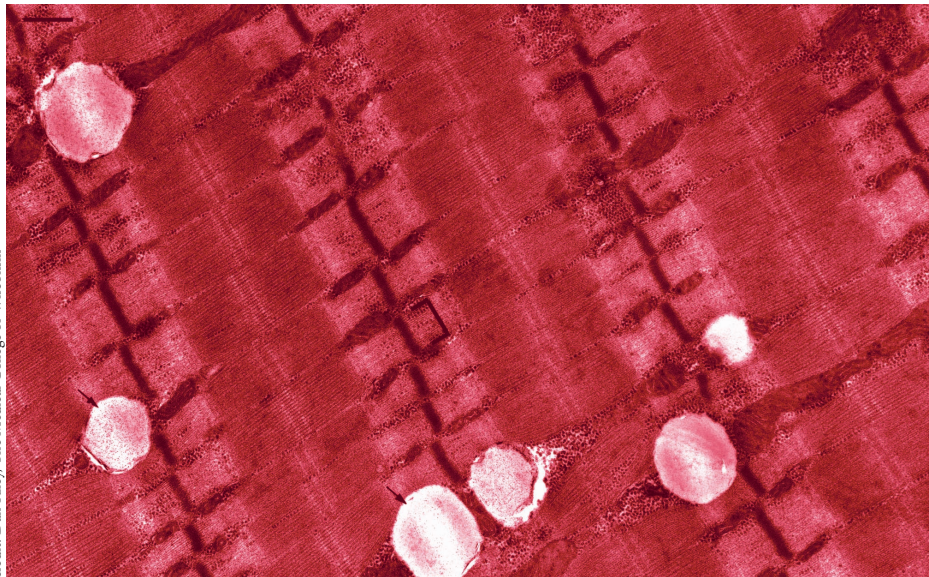
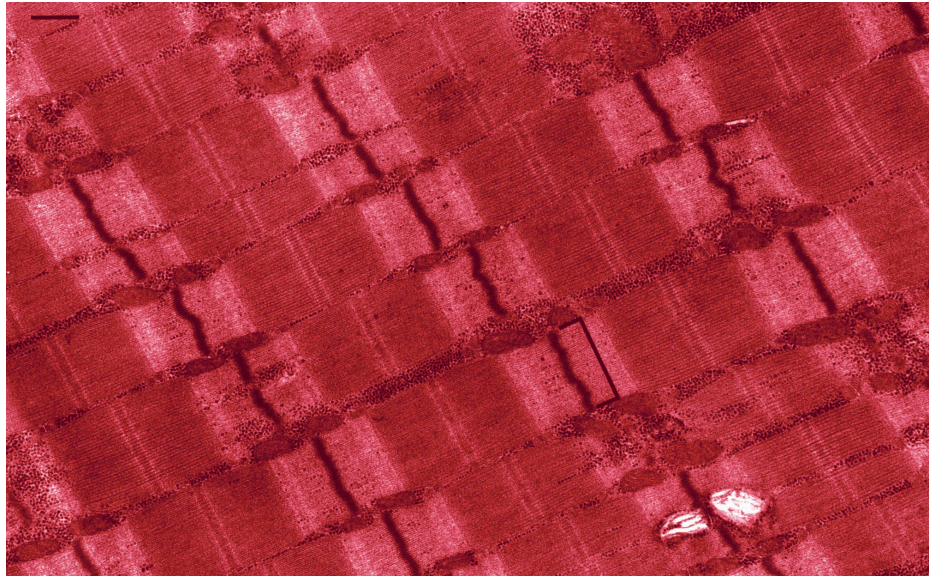
With the IRED, as well as the treadmill and the cycle ergometer, astronauts are better equipped to maintain their health while in space. Studies of their

Joint Research in Human Physiology

NASA is not the only federal agency interested in human physiology research, and NASA is benefiting from and contributing to what other organizations are learning. In fact, the space agency has 40 agreements to conduct joint studies regarding various aspects of human health and well-being with other federal agencies and organizations. Here are just a few:

- American College of Sports Medicine: musculoskeletal and exercise physiology research
- American Federation for Aging: the aging process
- Centers for Disease Control and Prevention: remote sensing technology in the areas of infectious disease surveillance, control, and prevention
- Department of Defense: mechanisms associated with blood volume and pressure regulation
- Department of Energy: radiation research
- Food and Drug Administration: diabetes research
- Juvenile Diabetes Foundation: research on the treatment of juvenile diabetes
- National Institutes of Health: a wide range of topics, from sensory motor functions, to application of robotics to neuromuscular adaptations, to spinal cord injury, to laser light scattering for early detection of cataracts; to basic understanding of vestibular functions.
- National Osteoporosis Foundation: educational outreach regarding osteoporosis
- National Science Foundation: basic research on psychological factors linked to spaceflight





The stimulus of gravity affects RNA production, which helps maintain the strength of human muscles on Earth (top), as seen in this section of muscle fiber taken from an astronaut before spaceflight. Astronauts in orbit and patients on Earth fighting muscle-wasting diseases need countermeasures to prevent muscle atrophy, indicated here with white lipid droplets (bottom) in the muscle sample taken from the same astronaut after spaceflight.

physiological systems are also helping scientists learn about what is required to maintain health on Earth. Hagan says, “What we have learned about response to microgravity is profound. When you go to space and spend a lot of time in microgravity without exercising, you basically end up wasting away. When we remove the stimulus of gravity, protein synthesis and calcium deposition in bone all stop, but the degradation processes all continue.

“But by making the muscles and bones work against high resistances, then we can better maintain the protein synthesis and the calcium status quo, and we can maintain stress on the cardiovascular system. Exercise is the single most important health maintenance method we currently have.” He says that it’s important on Earth, too. “Becoming highly sedentary is much like going to space. What we see in the sedentary lifestyle is exactly what happens when people spend a

lot of time in flight and don’t exercise. That’s why we all have to exercise.”

But exercise is an inexact science, and researchers still don’t know what magnitude of stimulus is required to maintain bone and muscle at preflight levels. So OBPR researchers are also looking for answers at a more basic level — genes.

Finding a Genetic Light Switch

Kenneth Baldwin, an OBPR principal investigator at the University of California, Irvine, and chair of the OBPR Biological and Physical Research Advisory Committee, is conducting research on how reducing the stimulus of gravity affects production of the RNA that the body uses as a blueprint for making muscle proteins. Muscle proteins are what give muscles their strength, so when the RNA blueprints aren’t available for producing new proteins to replace old ones — a situation that occurs in microgravity — the muscles atrophy. Baldwin, who serves as team leader on muscle research at the National Space Biomedical Research Institute, explains why this information is important to astronauts: “When the skeletal muscle system is exposed to microgravity during spaceflight, the muscles undergo a reduced mass that translates to a reduction in strength.” When this happens, muscle endurance decreases and the muscles are more prone to injury, “so individuals could have problems in performing extravehicular activity [space walks] or emergency egress because their bodies are functionally compromised.”

During spaceflight investigations conducted from 1991 to 1997, Baldwin studied the development of skeletal muscles in rodents during critical developmental periods following birth. He and his research team found that in microgravity, “muscle that would normally be programmed to become antigravity muscles [such as leg and back muscles] was not producing the appropriate type of motor proteins in those fibers that basically are designed for the body to oppose gravity. The specific genes [that trigger slow motor protein production in those muscles] were not activated.” Baldwin suspected that these same genes were being shut down in astronauts while they were in microgravity, reducing the key proteins produced by antigravity muscles and thereby contributing to atrophy.

So Baldwin and his team began studying the effect of microgravity on transcription, translation, and protein degradation. Transcription is the process of using a DNA molecule as a template to construct a messenger RNA molecule that ends up with the same genetic information as the DNA. Translation is the process of then using the genetic information in the



messenger RNA (mRNA) to form a protein molecule. Baldwin explains the connection between these two processes and degradation, the decomposing of proteins at the end of their life cycle, and atrophy: "When we talk about the flow of information for any given gene, we have what is called 'promoter' activity [such as the presence of gravity], which keeps the gene turned on so it produces more mRNA [transcribes], and then that mRNA now gets translated into the building of a protein. That protein now continues to serve some functional role, and then over time that protein is targeted for degradation through the activation of other important genes."

Baldwin is looking at the genes connected to a specific motor protein, called a myosin-heavy chain. He explains, "Myosin is the most abundant protein that is expressed in muscle, and it is a structural motor protein that serves as the key regulatory protein for bringing about the process of contraction. It regulates the force that is built up in the muscle when the muscle is induced to contract by the nervous system, and it regulates the intensity of the contraction, and hence the power-generating capability of the muscle."

Baldwin says that weight bearing, as it occurs normally on Earth, keeps the slow myosin gene active in the antigravity muscle fibers, and when there's no regular force production, the gene gets shut down. So Baldwin, too, is looking for the amount of force

necessary to keep muscles strong. "If I make the muscles contract five times a day with very high amounts of loading on them," he asks, "is this enough to keep the gene turned on that will keep the protein expressed that will keep the fiber integrity there?"

Baldwin foresees the possibility of using gene therapy as another countermeasure to muscle atrophy: "It may be that we will find certain factors that are pivotal in controlling the gene [connected to the myosin-heavy chain]. If we understood basically how to turn those factors on, you could end up controlling muscle strength through pharmacological intervention rather than using work."

"There's a practical side to this," he continues. "We may find, for example, that in order to keep the

muscle integrity of individuals in space, they may have to exercise eight hours a day. That's not cost-effective. So the question is, could astronauts take a pill or some other type of prescription that would enable them to have that factor that acts in concert with exercise, so with 40 minutes of

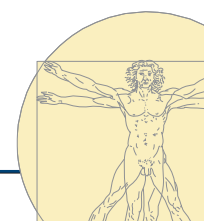
exercise a day, coupled with this 'magic pill' they take, they could maintain their homeostasis, or equilibrium?"

The answer to Baldwin's questions could help keep astronauts' muscles strong during spaceflight to prepare them for returning to Earth's gravity, maintain terrestrial athletes' muscles at top performance levels, and preserve the muscles of humans fighting muscle-wasting diseases.

OBPR researchers are studying the effects of microgravity on how messenger RNA molecules form protein molecules that maintain muscle strength. Practical applications of his research could lead to finding how gene therapy (through pharmaceuticals) and exercise could work in concert to keep astronauts' muscles strong.

"If I make the muscles contract five times a day with very high amounts of loading on them, is this enough to keep the gene turned on that will keep the protein expressed that will keep the fiber integrity there?"

— Kenneth Baldwin
OBPR principal investigator



OPG Is A Physiological Regulator of Bone Density

Normal OPG



Extra OPG



Lack of OPG



OPG could be an effective countermeasure to bone loss experienced by astronauts and by patients with osteoporosis.

The Bare Bones of Spaceflight

OBPR scientists are also studying how to minimize bone loss, another condition experienced by astronauts. Ted Bateman, a principal investigator and director of biomedical research at BioServe Space Technologies, a NASA-sponsored commercial space center, describes this effect: "When you remove gravitational loading, bones no longer sense the stresses and strains that are normally experienced here on Earth. As a result, astronauts are subjected to an accelerated rate of bone loss, losing between a half of 1 percent and 2 percent of their bone mass per month," or 6 to 24 percent a year. By contrast, bone loss in women with Type I (hormone-related) osteoporosis, a condition characterized by a decrease in bone density and an increase in porosity and fragility, is 3 to 4 percent a year, and less in men and women with Type II (age-related) osteoporosis.

Bateman, who is based at the University of Colorado, Boulder, has been using mice in ground-based studies to learn what happens to bones in microgravity. He is partnering with Amgen Inc. to examine a potential countermeasure for the related bone loss. The mice are positioned in a ground-based procedure to mimic reduced gravity conditions in space and are treated with osteoprotegerin (OPG), a naturally occurring

protein that is a potent regulator of bone metabolism. OPG is being developed by BioServe's commercial partner, Amgen, as a pharmaceutical drug and is currently undergoing clinical trials with the Food and Drug Administration. In his ground-based studies, Bateman found that OPG maintained the mechanical strength of bones in mice in simulated microgravity when they were treated with levels of OPG equal to that of a mouse in normal gravity.

Now Bateman is examining the osteoporosis that mice experience in actual microgravity and whether OPG can minimize or even prevent this bone loss. In December 2001, the flight-based portion of the BioServe/Amgen research went to orbit as a space shuttle experiment on STS-108. For this experiment, Bateman and Paul Kostenuik, the Amgen principal investigator, injected 12 mice with OPG, and another 12 mice with a placebo. OPG binds with another protein in the body, OPG-ligand. By doing so, OPG prevents osteoclasts (bone absorbing cells) from removing too much of the bone that osteoblasts (bone-forming cells) are producing. A proper balance between osteoclasts and osteoblasts is fundamental to development and maintenance of bone health. Extra osteoblast activity in children allows for bones to grow, while after maturity, approximately equal activity of the two cell types keep bone formation and absorption in

credit: Amgen Inc.

balance. Bateman explains the importance of this function: “With astronauts, it is pretty clear that microgravity uncouples bone formation and bone resorption, so there exists an inhibition of bone formation. But most of the loss in bone mass is going to come from an increase in bone resorption.” Finding an effective countermeasure to this increased resorption could help astronauts maintain their bone density and strength while they’re in space.

An OPG treatment also could potentially help people on Earth with osteoporosis. According to the National Osteoporosis Foundation, 10 million people in the United States have been diagnosed with this disease, with another 18 million Americans at risk with low bone density. Eighty percent of patients with osteoporosis are women. Osteoporosis is responsible for more than 1.5

million fractures every year. Bateman describes the seriousness of the condition: “Osteoporosis is a disease without symptoms. You don’t have any indication that you have it until you get a bone density scan or until you get fractures. People in their 60s or 70s

could be out playing golf, playing tennis, or walking several miles a day, and suddenly get a hip fracture or a vertebral fracture, and become bedridden.” Bateman hopes the BioServe/Amgen research with mice will lead to an effective treatment for osteoporosis that could impact thousands of lives, both in space and on Earth.

Learning the Basics of “Moon Face”

Another study that could help astronauts is the work of John Tarbell, of Pennsylvania State University. Tarbell is using a cell culture model to find the cause of and countermeasures for “Moon face,” a shift of fluids to the upper body, creating a rounder, fuller face.

Looking to cells for answers to some of the mysteries of how spaceflight

affects the bodies is not such an unusual research move. Kathie L. Olsen, OBPR acting associate administrator, explains, “In terms of understanding human physiology, you can look at the human on down [to a subcellular level], but you can also be reductionistic — [start at the smallest level] and come up.” Scientists like Tarbell in the microgravity fluid physics discipline are working at the cellular level. Fluid physics discipline scientist Bhim Singh, of Glenn Research Center, explains the importance of research at this level: “While a great deal of progress has been made in understanding the changes in human physiology caused by microgravity, and some effective countermeasures have been developed, little is really understood about the fundamental mechanisms responsible for the changes. Understanding fluid

physics and transport at the cellular level in the microgravity environment will be crucial to identifying the factors responsible for creating adverse physiological problems.”

Tarbell is learning the causes of Moon face by studying the endothelial cell layer, which lines blood vessels from the aorta to the capillaries.

These cells provide the principal barrier to transvascular transport, the passing of water and solutes between blood and underlying tissue. On Earth, these cells are continuously exposed to the mechanical shearing force and the pressure imposed by blood flowing over their surfaces, and they are adapted to this environment. When the cardiovascular system is placed in microgravity, which affects fluid flow, pressure in the blood vessels changes, and the shearing force is eventually reduced, which increases the endothelial cell layer’s hydraulic conductivity, or its ability to transport water and solute, making the layer much less effective as a

barrier. Tarbell proposes that this situation allows transvascular transport, causing the fluid shift that occurs in humans in microgravity.

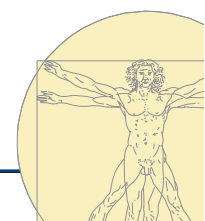
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Astronauts experience a cold-like sinus and nasal stuffiness and a rounder, fuller face called “Moon face” (right) when the barrier that normally prevents fluids from passing from blood vessels into surrounding tissues on Earth becomes ineffective in microgravity.

“Understanding fluid physics and transport at the cellular level in the microgravity environment will be crucial to identifying the factors responsible for creating adverse physiological problems.”

— Bhim Singh, fluid physics discipline scientist



The International Space Station – The Most Unique Laboratory in

Like a science-fiction movie come to life, the ISS is a research lab in the sky where experiments can be run for months, not days, and the world of microgravity is the norm, not the exception.

What makes the International Space Station (ISS) unique? Location, location, location — in low Earth orbit. Researchers now have a laboratory where they can study various scientific phenomena in a continuous microgravity environment. This will be especially useful for life scientists, who will finally be able to study the effects of microgravity on plants and animals for long durations and over multiple generations. In the sections below are descriptions of how scientists working under the auspices of the Office of Biological and Physical Sciences (OBPR) are already using this new laboratory.

The **Bioastronautics Research Division** is charged with biomedical research and human support technology development. Scientists perform biomedical research that will help space-traveling humans in two areas: (1) living and working in space safely and in good health, and (2) recovering to normal function on their return to Earth. In addition, scientists gather information on how humans adapt to spaceflight.

The research conducted in microgravity can also benefit groups

of people on Earth, including the elderly and those who live and work in remote locations where medical treatment is less accessible or where usual access to medical facilities is cut off by natural disasters, such as floods, or by human intervention, such as in times of conflict. In addition to biomedical research, other studies, such as the development of new technologies for the detection of any harmful elements in and purification of air and water, which are essential for maintaining health in space, can be translated into practical Earth applications.

Bioastronautics researchers have a number of ongoing and planned experiments aboard the space station. Several of these projects are designed to study the bone and muscle loss that occurs during spaceflight, with the goal of counteracting those effects. The Hoffman Reflex experiment, which arrived on station with the Expedition 2 crew in February 2001, investigates motor neuron function by examining the effects of microgravity on the ability of the spinal cord to react to stimuli. If the spinal cord experiences reduced excitability during spaceflight, then motor neuron function decreases and

muscles lose tone, even with exercise. Because astronauts have limited time for exercise, researchers would like to determine the cause of and possible solutions for this loss of spinal cord excitability.

Similarly, in-flight bone loss will be studied using quantitative computed tomography, a three-dimensional assessment technique that allows the inner and outer portions of the bone to be examined separately, and dual-X-ray absorptiometry, which provides a two-dimensional measurement of the mass of the entire bone. Astronauts on Expeditions 2 through 6 will participate in this study, which began in February 2001 and will continue through October 2002. Control subjects on Earth will also be a part of the study. Researchers plan to compare the results obtained from astronauts pre- and postflight with those of the control subjects and to track the distribution of bone loss during spaceflight and the extent of recovery afterward.

Studies of pulmonary function during space walks, orthostatic intolerance (the inability of the body to regulate cerebral blood pressure upon standing up; see page 14), and kidney stone formation (see *Space Research*, vol. 1, no. 1, p. 27) are also being conducted aboard the

ISS. Future experiments will include a skeletal muscle biopsy study, as well as mobility and immunology studies. Each of these experiments is being undertaken to better understand specific phenomena that occur during spaceflight; however, the results could be used to develop treatments for conditions on Earth as well.

Another phenomenon being studied is exposure to neutron radiation, which is specific to spaceflight. Having the ISS as a platform on which the physiological effects of such radiation can be studied over time will enable researchers to better develop protective measures for astronauts as well as for radiation workers on Earth.

Bioastronautics researchers are also studying the psychology of living and working in space in small groups and confined areas (see *Space Research*, vol. 1, no. 1, p. 12). The psychological effects of living and working in the unique environment of the space station cannot be replicated on Earth, and the fact that station crewmembers spend up to four months at a time on the station provides researchers with a prime

**What makes the
International Space Station unique?
Location, location, location.**

the Universe

opportunity to delve into small-group interactions in a distant, isolated, and at times hazardous environment.

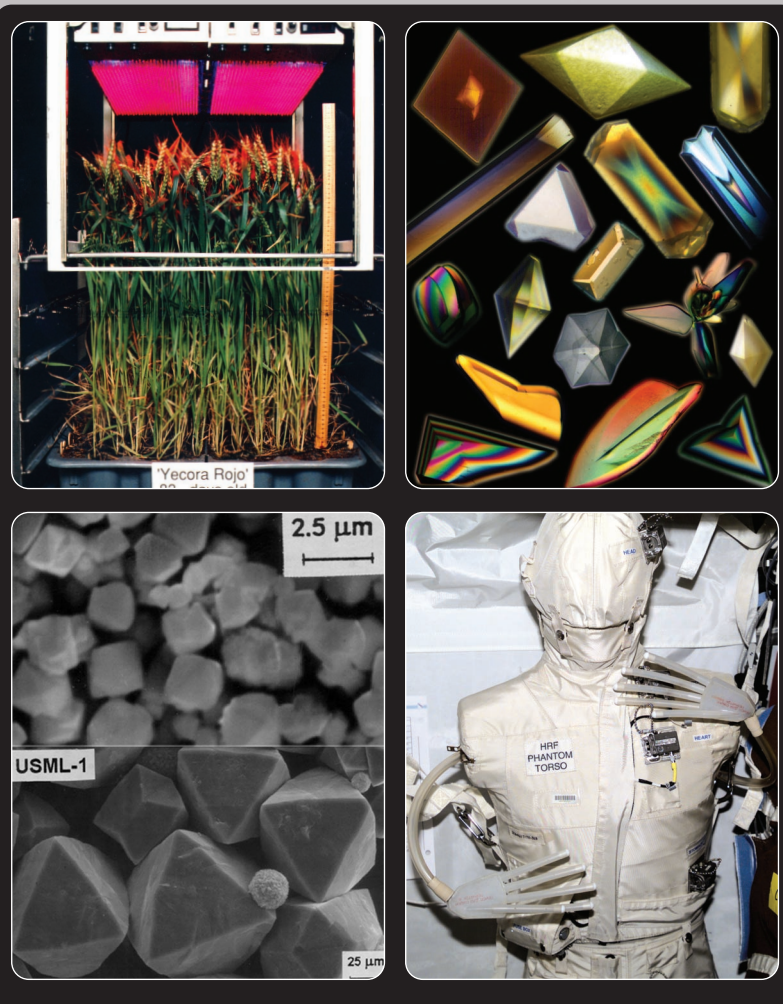
Research in the above areas will be carried out using the equipment in the Human Research Facility (HRF) Rack 1, already in place on the station, and HRF Rack 2, which will be transported to the station with the Expedition 5 crew in June 2002. The new rack will provide additional storage areas and services for experiments on the physiological, behavioral, and chemical changes in the human body during spaceflight.

The Fundamental Space Biology Division conducts research in a microgravity environment to better understand fundamental biological processes. This information can then be applied to solving problems associated with long-duration spaceflight, understanding the role of gravity in the development and functioning of living systems on Earth, and expanding our knowledge of basic biology on Earth and in orbit. Researchers are developing experiments to be conducted aboard the ISS once the appropriate hardware is in place.

The Avian Development Facility (ADF), which will allow researchers to better understand the effects of reduced gravity on the development of bird embryos, was flown on STS-108 in December 2001. One of the two experiments conducted in the ADF studied the development and function of the avian otolith system, the system by which organisms orient their head position and movement in relation to gravity. The second experiment sought to define the effects of spaceflight on embryonic skeletal development.

Although ISS budget and construction constraints have required some experiments to be deferred from their original deployment dates, fundamental space biology researchers are still planning micro-gravity experiments to study the long-term effects of exposure to the spaceflight environment on biological processes at all levels of biological functioning, from the cell to the whole organism.

The Physical Sciences Division conducts both applied and fundamental research. It uses the microgravity environment of orbit to study how



credit: NASA

In a world of its own, the ISS provides scientists with the opportunity to conduct long-term research in microgravity. The various OBPR research divisions have projects either in progress on the station or in the final stages of preparation. Clockwise from top left, research projects as diverse as growing plants over multiple generations, growing protein crystals, detecting neutron radiation, and developing hardware to grow zeolite crystals for commercial purposes will take advantage of this one-of-a-kind laboratory in the sky.

physical, biological, and chemical processes function in both the biotic and abiotic realms. Physical sciences research covers a wide range of fields, from atomic physics to combustion science to tissue engineering.

Several fundamental physical science experiments are currently being conducted aboard the ISS. One such study is of binary colloidal crystals. A colloid is a system of small particles suspended in a fluid. Colloidal systems can form crystalline and glassy solids. The goal of the Physics of Colloids in Space experiment being conducted by Dave Weitz, of Harvard University, is to better understand how these unusual systems can be manipulated to create new materials

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Research Update:

Bioastronautics Research

Dizziness in Astronauts Leads NASA Researchers to Find Genetic Cause for Orthostatic Intolerance

Studies of astronauts before, during, and after spaceflight not only will help stop the dizziness that occurs after returning to gravity but may also help many people on Earth who get dizzy simply when standing up.

It is a regular occurrence in families — the inheritance of a trait from grandparent to parent to child. Often it's something easily recognized, like red hair or blue eyes. Occasionally it's something more serious, like a medical condition. The trait can be the result of a

genetic defect that happened generations ago and has been passed down through the family ever since. Diabetes, sickle-cell anemia, and color blindness are conditions caused by genetic defects that frequently run in families. Most families don't realize that their medical trait is the result of a genetic defect, and they wouldn't expect the link between their trait and a genetic defect to

be discovered through NASA research. But such was the case with the disorder orthostatic intolerance (OI), which causes individuals to feel lightheaded when they stand up from sitting or lying down.

Now why, you might ask, does studying people with OI help the space program? It helps because many astronauts experience OI for the first few days after they return from spaceflight, and NASA scientists want

to find out why. David Robertson, director of the Center for Space Physiology and Medicine at Vanderbilt University, had been studying OI in ground-based patients for many years. Along with his colleagues, Robertson designed several experiments for the Neurolab space mission in April 1998 to try and find the cause of OI in astronauts. They hope that this research will uncover the cause or causes of OI and thus protect both astronauts and the many people who are chronic sufferers of OI from experiencing this disorder.

What Is Orthostatic Intolerance?

Orthostatic intolerance is a dysfunction of the autonomic (involuntary) nervous system that affects, in addition to the astronauts, an estimated 500,000 people in the United States, according to the National Dysautonomia Research Foundation. Normally, when a person stands up, the autonomic nervous system automatically adjusts the cardiovascular system to maintain the necessary blood pressure and flow, especially to the brain. When a person with OI stands up from a sitting or lying position, the autonomic nervous system malfunctions, blood flow and pressure are not properly maintained, the brain does not get the blood flow it needs, and the person experiences symptoms ranging from dizziness and nausea to blurred vision and heart palpitations.

Robertson explains why the simple act of standing up can be so stressful on the body: "I think the answer to that lies in the fact that standing up is relatively new from an evolutionary standpoint. You've got to pump blood all the way up to the top of a 5-foot or 6-foot person to get the

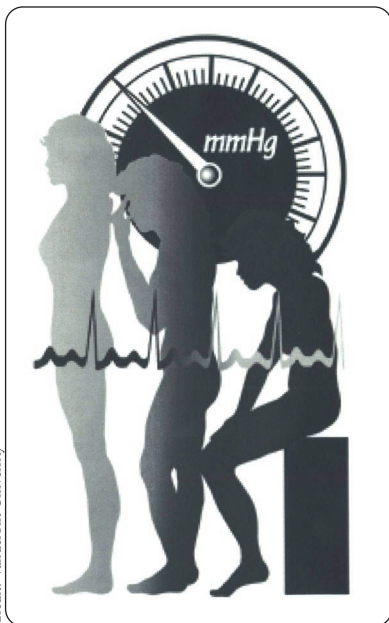
brain plenty of blood. It's a lot easier to pump the blood when there's no gravity between the heart and the brain than it is the other way around. Moreover, you've got those legs down there where blood can pool, and if it pools down there in the legs, not as much comes back to fill the heart, and so the heart has to pump more often in order to do the same thing." In people with OI, these effects can range in severity from annoying to severely disabling, preventing some sufferers from holding down jobs and living regular lives.

Prior to the early 1990s, doctors frequently misdiagnosed OI. "I'm sorry to say that 20 years ago I probably told young women who came to see me about this problem . . . [that] they were deconditioned and they needed to get more exercise," says Robertson. "What changed my view was a finding in the early 1990s that cerebral blood flow, blood flow to the brain, fell more in these patients than in normal subjects. Even though the blood pressure was just as high when they stood, their brain blood flow fell when they stood, more than it should. And that's what keyed me in. We used to think if the pressure was okay when you were standing, your brain would do fine. In this group of patients [ones with OI], that proved not to be the case."

Expected Results

When Robertson and his colleagues set up the experiments for the Neurolab space mission, they thought they knew what they would find. "We were focused on the disease being caused by a partial damage or dysfunction of the autonomic nervous system, and when those nerves in the lower part of the body are not doing their job, blood pools there," says Robertson.

From previous ground-based experiments, Robertson thought the expected dysfunction of the autonomic nervous system would manifest itself as a below-normal level of neurotransmitters in the blood. Neurotransmitters, such as norepinephrine and epinephrine, are chemicals that help the sympathetic nerves constrict blood vessels. Sympathetic nerves are part of the autonomic



Orthostatic intolerance manifests itself as a drop in blood pressure and flow to the brain when a person stands from a sitting or lying down position. (Pressure is measured in mmHg, or millimeters of mercury.)

Credit: Vanderbilt University

nervous system. It is this constriction that maintains a sufficient pressure and flow, especially in blood vessels that run up the body and against the pull of gravity. A low level of these chemicals would account for lower activity in the autonomic nervous system. The blood vessels would not constrict enough to keep the pressure sufficiently high to move the blood up the body and into the brain. This would cause blood to pool in the legs and reduce the total blood volume available to the brain. As the body's priority is to supply blood to the heart first, the brain does not get enough and the body experiences orthostatic intolerance.

Robertson's results, however, revealed that OI was primarily caused by elevated levels of neurotransmitters, specifically norepinephrine, in the blood. Robertson explains what these increased levels do to the body: "First it raises the heart rate and causes constriction of all blood vessels; [then as a result,] there is a secondary loss of blood volume [to the brain], and this creates a vicious cycle." The higher levels cause the blood vessels to constrict too much, with the same results of retarded flow to the brain. The effects of this cycle are what cause orthostatic intolerance.

For astronauts, this increased level appeared to be caused by the decrease in blood volume that normally occurs when they are in space. "Low blood volume can make the sympathetic nervous system work harder," explained Robertson, "... and when the sympathetic nervous system works harder, the plasma [blood] norepinephrine level goes up because sympathetic nerves release norepinephrine." Astronauts do not experience the symptoms of orthostatic intolerance until they return to gravity. Once on Earth, OI symptoms only last until the astronauts' blood levels return to normal. When this happens, the cycle is broken and they no longer experience orthostatic intolerance.

For ground-based patients, the causes and effects were not as obvious. Armed with the results from the Neurolab space mission experiments, Robertson and his colleagues revisited the data from their regular patients. They discovered that some patients being studied had several family members who also had OI. "We saw that some patients resembled the astronauts in the way their bodies operated, and some



Credit: Vanderbilt University

David Robertson, director of the Center for Space Physiology and Medicine at Vanderbilt University, was trying to find the cause of orthostatic intolerance (dizziness) in astronauts when he discovered a genetic mutation that causes the disorder in some ground-based patients.

looked very different. Those that looked very different seemed to have a hereditary component, and it was through that comparison that we nailed down the fact that a particular gene was abnormal," says Robertson.

Common Factor Found

From the Neurolab results, Robertson knew that the common factor among astronauts and Earth-based subjects was an elevated level of norepinephrine in the blood. This could only have two causes: one, that the body released more norepinephrine than is normal; or two, that the body did not remove the excess norepinephrine at the normal rate. The first cause seemed to be what happened with the astronauts and appeared to be related, at least in part, to the reduction in blood volume during spaceflight. The second cause appeared to have its roots in a defect of the norepinephrine transporter (NET) function. The NET is a protein, a coiled string of amino acids arranged in a specific sequence that is determined by an individual's DNA. A mutation in the code can cause the resulting NET protein to malfunction. The NET's job is to remove excess norepinephrine from the blood, and the malfunction results in an above-normal level of the neurotransmitter.

Once Robertson realized that the NET malfunction was caused by an abnormal gene, the next step was to locate the gene. He worked with Randy Blakely, director of the Center for Molecular Neuroscience at Vanderbilt, to find and characterize the mutation in the gene that codes for the NET. Nancy Flattem, a medical student from

Blakely's group, found the defect — one "letter" of the DNA code that determines the sequence of amino acids in the NET was different from the normal gene. This mutation causes the amino acid in position 457 to be the amino acid proline instead of the amino acid alanine, resulting in a 98 percent failure of function for the NET. This failure prevents the NET from doing its job, too much norepinephrine stays in the blood stream, and the patient experiences orthostatic intolerance.

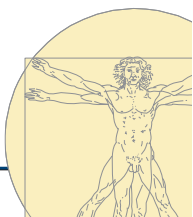
These findings mark the first time a genetic defect has been linked to a disorder of the autonomic nervous system. This discovery could help scientists design drugs and treatments that might significantly improve the quality of life for sufferers of OI, both temporary, like the astronauts, and chronic, like the ground-based patients.

Moving toward this goal will take time, however. While much has been learned about orthostatic intolerance due to the NASA research, Robertson and his colleagues still have a lot of work ahead of them. "We're looking for other genetic causes," he says. "We're looking for problems in the body's handling of blood volume. And we're looking for problems in how the brain controls the heart and the cardiovascular system."

As to how to stop the symptoms that the astronauts were experiencing, Robertson says, "I think better ways to maintain hydration and normal autonomic control in the microgravity environment will be the critical factor." How this can be done will, of course, be the goal of future research. There are a lot of questions still to be answered. With the opportunities soon to be available on the International Space Station, Robertson and his colleagues will have the chance to find those answers.

Carolyn Carter Snare

Robertson's research team included Italo Biaggioni, Rose Marie Robertson, André Diedrich, F. Andrew Gaffney, Andrew Ertl, and graduate students Sachin Paranjape and Robert Carson. These research results were published originally in Robertson, D., et al. (2000). Orthostatic intolerance and tachycardia associated with norepinephrine-transporter deficiency. *The New England Journal of Medicine*, 342(8), 541-549. For additional information on Robertson's space research, visit <http://www.mc.vanderbilt.edu/gcrc/space/>. For additional information on orthostatic intolerance, visit <http://www.ndrf.org/orthostat.htm>.



Research Update: Fundamental Space Biology

Will Space Travel Affect Reproduction?

Studies of sea urchin sperm indicate that gravity, or the lack thereof, could indeed have a significant effect on fertilization in space.

Colonizing other planets and living and working in space for entire lifetimes were once the stuff of science fiction, but these days spaceflight itself has become somewhat routine, and space stations (*Skylab*, Russia's *Mir*, and recently the



The purple sea urchin, *Strangelocentrotus purpuratus*, is a widely used model for studying the biology of fertilization because the mechanisms of its sperm movement and fertilization are well-known. Sperm and eggs are collected during the spawning season. On the left, a spawning female sea urchin has deposited eggs, and on the right, a male sea urchin has deposited sperm.

International Space Station) have provided people with the opportunity to live and work in space for extended periods of time. People now speculate that the ability to explore and colonize other planets is simply a matter of time. But some practical issues that go with traveling to and inhabiting other planets must still be addressed. One of the most fundamental biological questions posed by space travel is that of the effects of microgravity on reproduction.

Sperm and Serendipity

In the course of a literature search pertaining to his research in the field of male reproductive issues and male contraceptives, NASA Principal Investigator Joseph Tash, of the University of Kansas Medical Center, came upon a paper by Ute Engelmann, of Medical Consulting in Munich, Germany, and her co-investigators. The paper described experimental results in which bull sperm motility was increased when subjected to freefall. Tash's discovery of the Engelmann article coincided with a NASA announcement seeking research

proposals for studying the effects of microgravity on the ability of species to reproduce, and Tash believed that his own research would benefit from a microgravity environment, so he submitted a research proposal.

Tash was interested in signal transduction, the process by which sperm are "told" to travel toward and fertilize an egg. He says, "We proposed to examine whether the signal transduction associated with the activation of sperm, and also the signaling that occurs in the sperm in association with signaling from the egg, were altered under the effects of microgravity." The proposal was selected for further ground-based studies and subsequently for flight studies.

Sperm vs. Eggs

Tash and his co-investigators chose to study sperm not only because that was where Tash's initial research interest lay, but also because sperm are very easy to collect, store, and study without affecting their function. With eggs, it's difficult to assess possible changes in their function resulting from the effects of microgravity without first fertilizing them. Notes Tash, "With sperm, you don't have to do that in order to get a good idea of whether they're working or not."

Sperm cells are considered to be terminally differentiated cells. They have just two functions: moving, and fertilizing the egg. Fertilization is not possible without sperm movement, so studying the fundamental ability of sperm cells to move is a relatively simple way of assessing sperm functionality.

For his research, Tash chose to use sea urchin sperm because the sperm are more uniform than sperm obtained from humans or other mammals, but their function and mode of movement are very similar to those of sperm from higher species. Tash notes that sea urchins are a long-standing, widely used model for studying the biology of fertilization. Common genetic origins, or homologies, between the sea urchin system and mammalian systems make the sea urchin a good model for obtaining basic information that can point to important

questions to be addressed by studying mammalian systems. Sea urchin sperm also provide the added benefit of survivability — they are able to tolerate delays that sometimes occur with flight research.

First Steps

To send the sperm into space, Tash and his co-investigators used the European Space Agency's (ESA's) Biorack facility, a multiuser biological research facility originally designed for shuttle missions. The investigators were supplied with the hardware a year ahead of time. They used this period to demonstrate that the hardware itself did not affect the outcome of their studies and that they could ask and answer the questions they wanted to before the experiment was manifested. "I think that's a real critical component of why we were so successful," says Tash.

A key aspect of the experiment was that the sperm were not in an active state — that is, they were not moving — when they were sent into orbit aboard the space shuttle. During fertilization in sea urchins, activation of the sperm occurs in less than a minute. Sperm are activated by a chemical process called phosphorylation, which sets off reactions within the sperm cells that start them swimming toward an egg. A separate chemical process stops sperm movement. During their preflight experiments, the researchers proved that the sperm could be collected and maintained in an inactive state for at least 20 hours before launch until the beginning of the experiment, which occurred a minimum of 20 hours after launch.

This preflight research involved developing new technology for sperm storage, which led to a patent for the team. The researchers have been able to adapt the technology for sperm from different species, and they hope that the technology will find application in the agriculture industry, specifically for the collection, storage, and transport of semen for use in breeding, such as when a farmer wishes to breed his cattle to a bull that is located in another part of the country.

A Moving Experience

The experiment involved looking at specific proteins associated with sperm motility. Sperm were held in chambers in the Biorack; each chamber held experiment hardware for six samples of sperm, and there were two chambers for each of the time points at which the sperm were examined (0, 30, and 60 seconds). Once the sperm were activated by the introduction of seawater, their movement was stopped at either 30 seconds or 60 seconds. The researchers were then able to use antibodies to compare how the proteins associated with motility changed at each of the time points.

"During our ground-based studies we found that two key sets of proteins, called FP 130 and FP 160, were likely associated with dynein, the main motor protein that is responsible for sperm tail movement," explains Tash, referring to a paper he published in *Biochemical and Biophysical Research Communications* in 1998 (see below for full reference).

"These proteins are phosphorylated [a phosphorous group is attached to them] during activation of sperm, which starts the whole chemical cascade within the sperm cell that leads to onset of motility. Under microgravity conditions, the phosphorylation of FP 130 and FP 160 occurred much more rapidly than it did under normal-gravity conditions," says Tash. This result is consistent with those obtained from the earlier sounding rocket experiments conducted by Engelmann. The researchers learned that the sperm will begin to move sooner and will move more rapidly in space than they will on Earth, but it is not clear whether faster sperm will actually lead to increased fertilization.

In a second flight experiment, Tash and his co-investigators were also able to examine the reaction of sperm to egg peptides that act as chemotactic factors to the sperm, guiding the sperm to the egg. The researchers discovered that the same proteins that were phosphorylated during the activation of motility were also modified in response to the presence of egg factors. In this second experiment, a delay occurred in the reduction of phosphorylation under microgravity conditions, meaning that the process that stops the movement of sperm occurred more slowly than under normal gravity. Tash explains, "This implies that microgravity could have an effect on

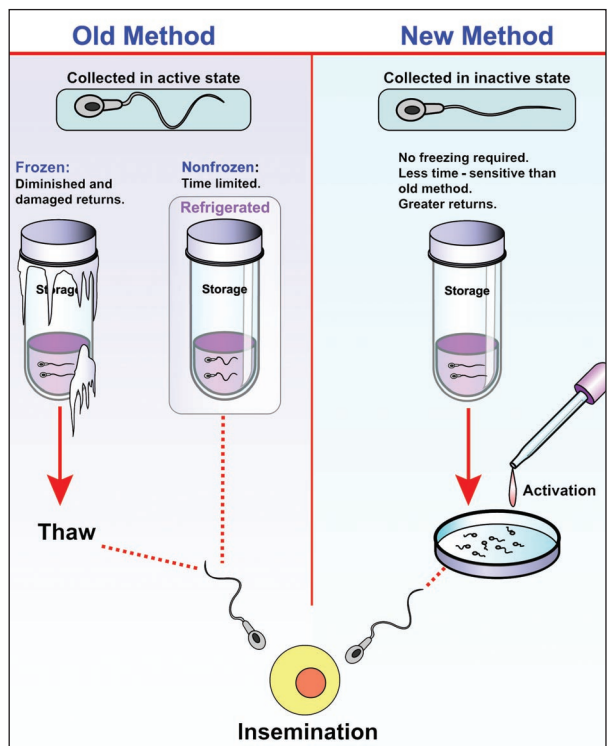
fertilization itself, on the efficiency and timing thereof."

Tash comments that the effects on phosphorylation could be either positive or negative — only further studies will tell. He remarks, "For example, the signal transduction [phosphorylation] that occurs during activation of sperm motility occurs faster, but because it's occurring faster, does that mean that it will also deteriorate faster? Because the sperm begin to move more quickly, does that mean that they will get to the eggs more quickly and fertilize better? There are all sorts of questions that this research raises that obviously have not been looked at in detail yet but hopefully will be."

Having found that microgravity caused an increase in sperm motility, Tash and his co-investigators decided to study the movement of sea urchin sperm and fertilization of the egg under increased gravity. Using a centrifuging microscope in Germany, Tash was able to study individual sperm in environments up to 5 g. He found that sperm motility was affected under hypergravity conditions as low as 1.3 g. The phosphorylation processes that were stimulated under microgravity were inhibited under increased gravity, and Tash observed a concurrent 50 percent decrease in sperm/egg binding and fertilization of the egg. The fact that both binding and fertilization were reduced by 50 percent under hypergravity conditions suggests that hypergravity exerts a primary effect on the sperm rather than on the egg. Had the primary effect been on the egg, then Tash would have expected to see a much greater drop in the egg response as compared with the drop in sperm/egg binding. Tash's experiments left him with no doubt that the level of gravity does indeed have a significant effect on sperm motility.

The Mammalian Connection

On the basis of these sea urchin sperm motility studies, Tash received another NASA grant to study reproductive issues in a mammalian system. His research team has done some preliminary work with rats under simulated microgravity. Early results, published in the *Journal of Applied Physiology* in 2001, indicate that sperm production is severely blocked after six weeks of simulated microgravity. So before continuing to study sperm motility,



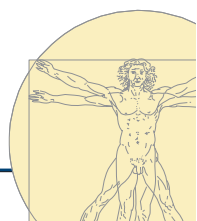
To be able to study the effects of microgravity on sperm motility, sperm had to be collected and stored in an inactive state prior to launch. Tash and his co-workers developed a new sperm storage method that did not require freezing of the sperm.

the investigators will now address the more basic issue of the effect of microgravity on sperm formation.

The issues surrounding the viability of reproduction in a microgravity environment will have a great impact on the ability of humans to succeed with long-term spaceflight and exploration in a microgravity environment. Tash's work has provided some answers to certain reproductive questions, but has also raised even more fundamental questions. Additional microgravity reproduction research, using mammalian and other systems, may supply solutions that will enable humans to live and work in space for extended periods.

Julie K. Poudrier

For additional reading, see Tash, J. S., & Bracho, G. E. (1998). Identification of phosphoproteins coupled to initiation of motility in live epididymal mouse sperm. *Biochemical and Biophysical Research Communications*, 251, 557-563; Tash, J. S., & Bracho, G. E. (1999). Microgravity alters protein phosphorylation changes during initiation of sea urchin sperm motility. *The FASEB Journal*, 13, S43-S54; Tash, J., et al. (2001). Fertilization of sea urchin eggs and sperm motility are negatively impacted under low hypergravitational forces significant to space flight. *Biology of Reproduction*, 65, 1224-1231; and Tash, J. S., Johnson, D. C., & Enders, G. C. (2002). Long-term (6-week) hindlimb suspension inhibits spermatogenesis in adult male rats. *Journal of Applied Physiology*, 92(3), 1191-1198. For additional information on Tash's research, visit <http://www.kumc.edu/Pulse/resources/shuttle/tash.html>.

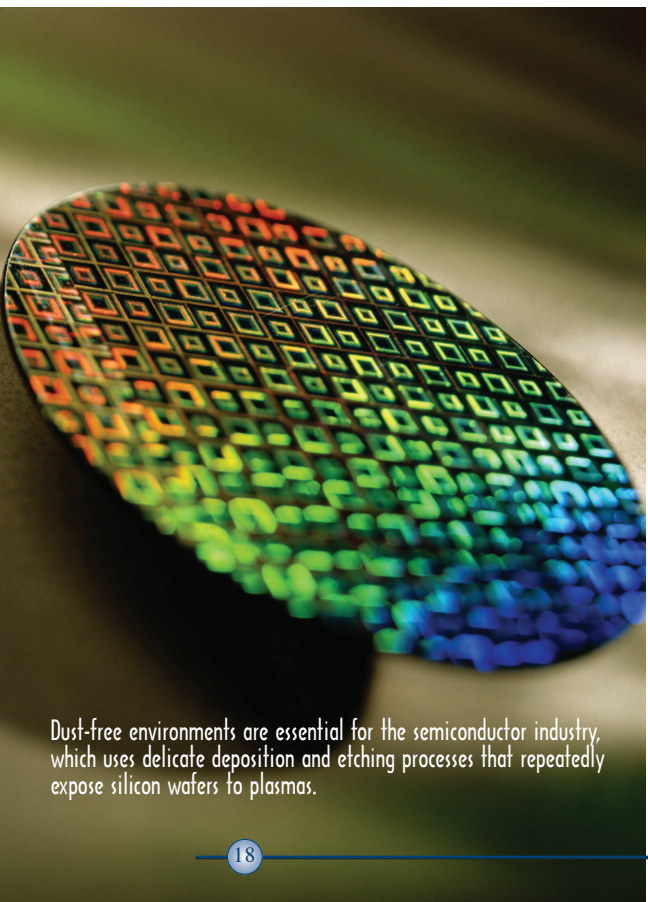


Research Update: Physical Sciences

Serendipity in the Laboratory: Dust Busters and Dust Seekers Find Common Ground

Thanks to new tools that allowed researchers to create dusty plasmas in the laboratory for the first time, researchers are using this variation of the fourth state of matter to understand phenomena such as the melting of a three-dimensional solid and the propagation of sound waves in a two-dimensional dusty plasma crystal.

It was a frustrating problem. Somehow, despite extreme precautionary measures, semiconductor chips were being contaminated with dust and ruined in the process. Manufacturers looked long and hard at what could possibly be causing the difficulty. And when the semiconductor industry discovered the culprit behind the mysteriously contaminated silicon wafers, researchers investigating dusty plasmas sat up and listened. What was vexing to the production of high-quality semiconductor chips allowed plasma researchers such as John Goree, of the University of Iowa, an opportunity to produce dusty plasmas in the laboratory for the first time.



Dust-free environments are essential for the semiconductor industry, which uses delicate deposition and etching processes that repeatedly expose silicon wafers to plasmas.

Plasma, Plasma Everywhere

Although the semiconductor industry is known for its efforts to provide absolutely dust-free “clean” environments for the manufacture of microchips, what was becoming clear was that while the usual sources of dust — operators’ skin cells flaking off, loose particles of dirt being kicked up by workers’ feet — were being adequately addressed, dust particles were settling onto microchips in some other way. The source of dust on the microchips was related to plasmas. Sometimes called the fourth state of matter, plasma is gas that has been ionized, which means an electric charge has released electrons from the nuclei of the atoms in the gas, leaving behind positively charged subatomic particles called ions, and unattached, freely moving electrons. The movement of the electrons in particular is greatly enhanced by the ionization process, as it acts to free the particles from their association with other subatomic particles in the nuclei of the atoms.

Naturally occurring plasmas are very hot gases, usually in excess of several thousand degrees Fahrenheit. Although they are less commonly found on Earth, they do make a rare appearance in the form of lightning. Also, the ionosphere, the layer just outside the Earth’s atmosphere, is a plasma. In fact, 99 percent of the universe is plasma. Cold matter like Earth is the exception, rather than the rule.

On Earth, the semiconductor industry uses artificial plasmas to deposit thin films onto silicon wafers or to remove layers of insulating or conducting metals from the

wafers’ surfaces in a process called etching. The deposition and etching processes are how transistors and interconnections are made on computer chips, and they require exceptional control and an absolutely clean environment. The ionized gas that is used in this process, however, might actually increase the likelihood that a chip will be contaminated with dust.

When random dust particles from the air enter the gas, they too are ionized, allowing them to move freely and remain suspended, instead of settling out of the plasma cloud. This is what researchers like Goree call a dusty plasma. Once the electric field is turned off, dust particles that have grown large enough fall to the surface of the silicon wafers, contaminating them and making them unusable as semiconductors.

While finding dust suspended in their plasmas can be tremendously costly for semiconductor manufacturers, their detection allowed Goree the needed setup to conduct experiments on dusty plasmas in a laboratory. Prior to the discovery of dust in the plasmas used in the semiconductor industry, no one knew how to make a dusty plasma in the laboratory, explains Goree: “The critical problem was what kind of instrument to use to make the dusty plasma. That’s when a semiconductor researcher discovered by accident a way of doing it.” Goree was involved with the field from the beginning, when the new kind of instruments began to be developed.

Add a Pinch of Dust

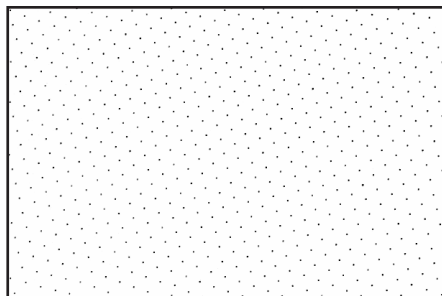
In his laboratory, Goree creates dusty plasmas using an apparatus with a design based on that of the equipment used in manufacturing semiconductors. “It’s a vacuum chamber with [gas and] two electrodes in it,” Goree describes. The electrodes are two flat metal plates. High-voltage electricity applied between the plates ionizes the gas in the chamber, resulting in a glowing discharge of primarily neutral gas plus some electrons and ions. Dust particles (in this case polymer microspheres less than 10 microns in diameter) are put into something that’s analogous

to a saltshaker. Goree explains, “We use polymer microspheres, but you could even use household dust if you wanted to.” The dust particles are shaken into the plasma, where they become electrically charged and will continue to be suspended in the plasma while electricity flows through the vacuum chamber.

Since the particles slosh around in the plasma, dusty plasmas are of interest to scientists working to understand the basic principles of fluid physics. Dusty plasmas are similar to colloids studied by fluid physics investigators examining the formation of ordered crystalline structures in suspensions of fine particles in liquid media. Like colloids, dusty plasmas consist of electrically charged particles of solid matter suspended in a fluid medium. While the medium for colloids in research investigations is typically water or water with added electrolytes, for dusty plasmas, the medium is a gas, such as oxygen.

Colloidal suspensions and dusty plasmas exhibit many of the same properties. For example, the particles of solid matter in a colloid are also electrically charged, so they repel one another, maintaining a certain distance between neighboring particles. The way that they achieve and maintain this separation is by arranging themselves at equal, fixed intervals in an array. The more the particles shift about with respect to their nearest neighbor, the more liquid-like the structure is said to be. More stable arrays, in which the particles move relatively little with respect to their nearest neighbors, form lattices or colloidal crystals. “Both the liquid-like and crystalline states can be achieved in dusty plasmas,” says Goree, “but we can also achieve another state that is gas-like, where the particles fly freely past one another and don’t ever stay near the same nearest neighbor.”

What’s also useful about dusty plasmas is that even in the solid or crystalline state, the movement of the particles in the plasma is less diminished by the surrounding medium than the movement of particles in a colloidal crystal. In a colloid suspension, the particles have to push around a lot of heavy liquid in order to move, losing a great deal of energy in the process. Particles in a dusty plasma can move about in the much less dense gas with less loss of energy.

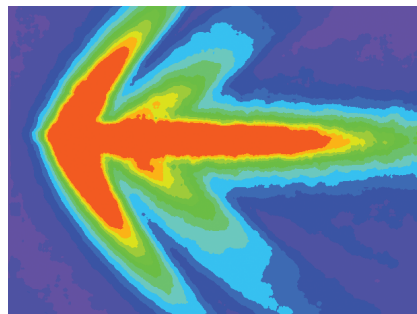


credit: University of Iowa

Dark black dots can be seen forming a regular hexagonal lattice pattern as each dust particle in this dusty plasma crystal is surrounded by six neighboring particles. The particles in dusty plasmas all repel one another because of their negative charges.

This diminished damping makes dusty plasmas particularly useful for observing phenomena such as the propagation of waves in a fluid. Goree explains, “As you speak, your voice is causing air molecules to be [repeatedly] compressed and then rarefied [stretched and thinned]. In a dusty plasma, because there is very little damping, the sound wave propagates very easily,” he says, making the propagation of sound waves much easier to study.

Goree is using the unique properties of dusty plasmas in a number of ways. His ground-based laboratory experiments have two focuses. The first is the melting of a two-dimensional dusty plasma crystal in which the particles have arranged themselves into a crystalline lattice. Adjusting the strength of the electric field applied to the plasma (and thus the repelling force of the charged particles) allows the particles in the dusty plasma to move so that they are no longer permanently adjacent to the same nearest neighbor. The particles become disordered as the lattice melts into a liquid phase. This process is called “two-dimensional” melting because gravity causes the particles to sediment into a horizontal, almost two-dimensional layer.



credit: University of Iowa

Sound waves near a loudspeaker cause air particles in their path to move in a repeating pattern. Goree’s research uses laser light to move solid particles, less than 10 microns in diameter, in a plasma crystal. Shown here, the resulting movement of the particles creates a pattern of sound waves similar to the Mach cone from a supersonic object in air.

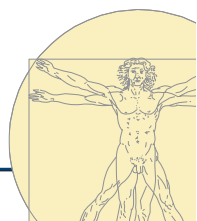
The second focus of Goree’s ground-based effort is studying the propagation of sound waves in a two-dimensional dusty plasma crystal. In this experiment, Goree uses laser beams to stimulate the propagation of the sound waves. The laser beams push the particles in the dusty plasma crystal in the same way that air molecules next to the cone of a loudspeaker are pushed by the sound coming out of the speaker.

“You might not think that light can apply a force to an object,” Goree notes. “For example, if you were to take a laser pointer and point it at your hand, you wouldn’t feel your hand being pushed away from the laser pointer, but it actually is applying a force to your hand. If you were to take that same laser pointer and point it at a particle that is smaller than 10 microns in size and is freely suspended, that particle would begin to move. Then if you chop that laser beam on and off, the particle will move forward and cease moving [correspondingly]. In that way, you can make an alternating or cyclical motion in the particle that is like the alternating or cyclical motion of the air molecule next to a loudspeaker.”

Goree also receives funding from NASA to sponsor his work as a co-investigator with German Principal Investigator Gregory Morfill, of the Max-Planck Institute, on a flight experiment designed to study melting in three-dimensional dusty plasmas in the low-gravity environment aboard the International Space Station (ISS). With the reduction of the forces of gravity that cause the particles in the dusty plasma to fall as sediment in ground-based laboratories, particles in the dusty plasma experiments conducted in space can fill a three-dimensional volume.

“Melting a three-dimensional solid is very different, microscopically, from melting a two-dimensional solid,” says Goree. “In space, we can study the melting process, observing microscopically where all of the particles are and how they move about with respect to their nearest neighbors, and we can do it not in two dimensions, which is kind of a synthetic thing under Earth conditions, but in three dimensions.” This ability gives researchers a better understanding of the melting process in three-dimensional solid matter.

The flight investigation, called the Plasmakristall Experiment (PKE), was



Research Update: Research Integration

Microgravity Helps Industry Characterize New Metal Alloys

From the sands of the Middle East to the vacuum of outer space, the search for improved metal casting technology continues, responding to the needs of an increasingly industrialized world.

The last time you took your new titanium golf clubs out for a few holes at the local course, it probably didn't occur to you that the clubs were manufactured using a process that is thousands of years old. Most golf club heads are made by casting, an ancient process in which molten metal is poured into a mold, allowed to solidify, then removed from the mold and either used as is or assembled with other castings to form any number of things. The process, which is believed to have originated in the Middle East more than 5,000 years ago, is still commonly used today. In fact, the foundry, or metal casting, industry is a flourishing business, producing everything from toothbrush holders to golf club heads to components of the space shuttle.

Since precise scientific knowledge about casting has been limited by interferences caused by Earth's gravity, the process is poised to benefit greatly from research in the microgravity environment on NASA's International Space Station.

While metal castings have been made for thousands of years, until recently, scientists still didn't know much about the fundamental

chemistry and physics of many of the metals that are used in the process. When working on a new casting process or testing a new alloy, foundry engineers usually had to use observation and trial and error to develop their methods and fine-tune their manufacturing processes. This method, while generally effective, nevertheless wastes time and expensive materials. By using precision scientific data and theoretical calculations to predict how a metal would react to the casting process, engineers could potentially reduce both wasted materials and lost time, thereby keeping pace with the increasingly sophisticated needs of the customers and keeping costs low enough to stay competitive.

Building a Vital Database

What the industry needed was a database containing thermophysical data for materials either currently in use or still under development. But most foundry companies are so small they cannot afford to do research themselves, so the American Foundry Society (AFS) partnered with NASA's Solidification Design Center (SDC), a commercial space center (CSC) at Auburn University, to begin the work. Tony Overfelt, director of the SDC, explains that without an accurate database "underpinning your process engineering and research and development, then your other work lacks credibility, since you can't convincingly interpret your data." Building such a database is one of the primary focuses at the SDC.

The SDC is one of 17 commercial space centers that are part of the Space Product Development Program, which is in turn part of the Research Integration Division in the Office of Biological and Physical Research (OBPR). The CSCs were formed to encourage the commercial development of space through partnerships


with business and academia. They are unique within NASA in that while their base funding is provided by NASA, research funding comes almost entirely from private industry. The SDC itself primarily conducts research related to the foundry industry.

Filling in the Gaps

Some of that research can be done on Earth. For the past 10 years or so, the SDC has worked with Ray Taylor, who runs TPRL Incorporated in West Lafayette, Indiana, and his team of mechanical engineers to do some of this ground-based research. Taylor started working with Overfelt and the SDC in the early 1990s while doing research at Purdue University. He specializes in the collection of basic materials measurements, helping the SDC to fill in some of the gaps in their database with highly accurate and reliable data.

Researchers at Auburn University have done some of the ground research as well. For example, the SDC has one of only four high-temperature viscometers in the world, enabling its scientists to measure the viscosity of aluminum alloys and steels on the ground and obtain data that are useful in designing casting processes.

Scientists at Auburn and elsewhere need to study the physics and chemistry of metals and alloys both in their solid states and during melting and solidification. Unfortunately, gravity interferes with some tests and some types of metals and prevents scientists from getting high-precision data. When the interference of gravity is suppressed, as it is during orbit on the space station, scientists have a more accurate picture of those characteristics and those metals. Overfelt explains, "For example, precise viscosity measurements of low-viscosity metals like aluminum are difficult in 1 g due to buoyancy convection effects. In addition, it's very difficult to obtain precise data about very reactive metals (titanium, magnesium, many super alloys) in crucibles [heat-resistant vessels used to melt materials] since they react with the very crucibles that contain them. Levitation experiments in low gravity provide extended times in the molten state without contact with crucibles." Were it not for this



Casting products range from the simple to the highly complex. Products as diverse as bolts, engine turbines, and jewelry are all made by the same process. Some castings, such as this turbine, are made in parts and must be welded together to form the final product.

Metal castings are made by heating up metal (often in crucibles such as these) until the metal is liquefied, pouring it into a mold, and then allowing it to cool and solidify. Studying such melting and solidification under microgravity conditions allows scientists to discover characteristics of the metals that are hidden under the influence of gravity.

opportunity for business to do microgravity research at NASA through the commercial space center program, the gaps in the metallurgy database of commercially important alloys might be permanent.

Going Containerless

While the SDC is involved in ground-based research, Overfelt and his colleagues are also working on experiments that will be flown on the International Space Station in 2003. They are sending up an electro-magnetic levitator, a containerless experiment device that levitates samples of metals and alloys which would otherwise react with their containers and thus contaminate the samples before data could be taken. While containerless research can be conducted on Earth, Overfelt asserts, "We'll be able to have much better control of boundary conditions [in orbit]. Nice spherical samples will behave in ways that allow us to reduce our raw data to actual thermophysical properties much more precisely and accurately." Each sample will be tested, first in its solid state and then in its molten state "to extract surface tension data . . . as a function of temperature," Overfelt describes. For this first launch, Overfelt is testing only pure elements so that he can compare the data he gets to established data he already has. This will enable his team to carefully validate the whole system on this first flight.

For future flights, the SDC plans to incorporate a flash diffusivity device that will measure how energy diffuses through the samples. The SDC is working with Anter Corporation, a small company in Pittsburgh, Pennsylvania. Anter makes thermal diffusivity devices and has modified one design so that they can "use the standard flash approach applied to spherical samples. Flash approach has [typically] been applied [only] to very thin samples," Overfelt describes. "We basically give it an impulse of energy on one side of the sample and measure how long it takes for that energy to diffuse through the sample. It tells us the thermal diffusivity of the material, one of the more important properties."

By building this database of material properties, the SDC engineering team is fulfilling its goal as part of the Space Product Development Program to bring

space research and business together for the benefit of everyone on Earth. Access to general information regarding research on nonproprietary alloys is available to anyone, without cost, from the SDC web site (see below). The SDC also functions as a testing lab for companies that need to have their metals or alloys characterized but do not have the facilities to do so themselves. Companies can receive the resulting data as proprietary data or allow it to be included in the general database. The benefits of the developing database to the metal industry as a whole are almost limitless.

Solid Plans for the Future

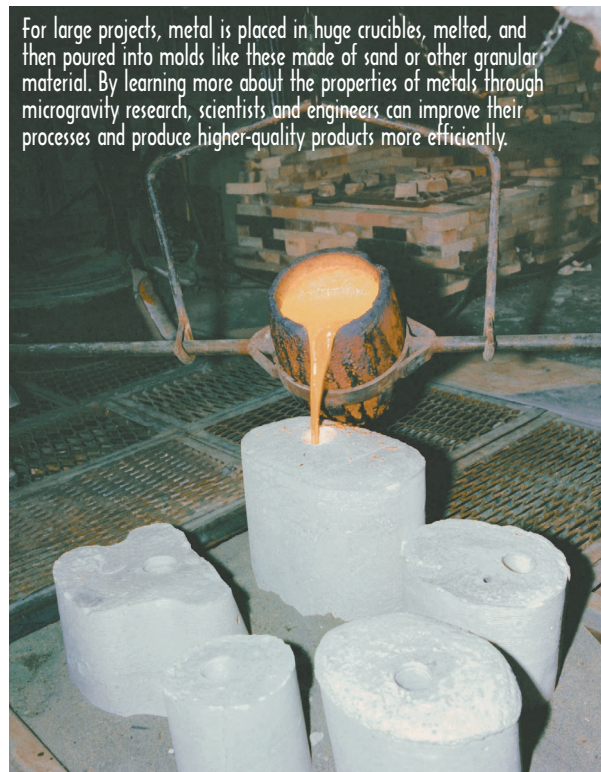
As Overfelt guides the SDC along its path of research, he keeps his eyes on the future. He intends to steer the SDC toward projects that will include work not only with the foundry industry but also with other companies that face similar challenges and as such might benefit from microgravity research. General Motors (GM) recently funded a project headed by Ken Williams, of Arena LLC in Albuquerque, New Mexico, that has resulted in groundbreaking software that will improve the quality of GM's casting molds. This software has enormous potential both for space research and for improving any manufacturing process that involves the flow of particulates.

"And so we're going to continue to work with the metal casting industry, expanding into the related manufacturing processes — any kind of a manufacturing process that has a fluid or a granular component where gravity has a role in distributing that process and then forcing the designers into a trial-and-error, empirical development

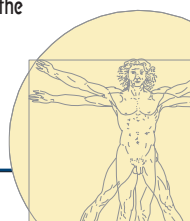
methodology," says Overfelt. "Anything that fits those parameters has the possibility of being improved by space experiments. I'm confident we'll be doing other projects that are not classical metal casting projects which are manufacturing-related and which do have applications to making metal components. I think the next 10 to 20 years of space research are going to help revolutionize many aspects of these businesses."

Carolyn Carter Snare

For large projects, metal is placed in huge crucibles, melted, and then poured into molds like these made of sand or other granular material. By learning more about the properties of metals through microgravity research, scientists and engineers can improve their processes and produce higher-quality products more efficiently.



For more information on Overfelt's research and the SDC, visit <http://metalcasting.auburn.edu> on the World Wide Web. For news on the commercial space centers in general, visit <http://commercial.nasa.gov>. For additional information on the American Foundry Society and the foundry industry, visit <http://www.afsinc.org>.



Education & Outreach

Principal Investigators Help Students Reach for Space

Principal investigators who take a personal interest in educational and public outreach activities are making a difference in how students experience scientific research.

Doing is better than just listening or watching. That's why some of the best supporters of future space missions may come from the ranks of young people who have experienced projects that engage them with space research and the principal investigators (PIs) who are conducting that research. One of the top goals of the Educational Outreach and Public Outreach Programs of the Office of Biological and Physical

Research (OBPR) is facilitating increased PI participation in its educational and public outreach activities. This personal involvement is valuable in motivating student interest in pursuing science, math, technology, and engineering careers, as well as in increasing general public understanding of NASA's research. This issue of *Space Research* highlights three investigators who not only lead great research, but also inspire students.

Martin Glicksman: USMP – 4 Leads the Way

One of the most successful OBPR outreach activities centered on the third flight of the Isothermal Dendritic Growth Experiment (IDGE) on the fourth United States Microgravity Payload mission (USMP-4) in 1997. During the shuttle flight, PI Martin Glicksman, of Rensselaer Polytechnic Institute, and Co-Investigator Matthew Koss, now at the College of the Holy Cross in Massachusetts, set up a remote payload control center for the experiment on campus at Rensselaer. This part of the outreach activity allowed undergraduate and graduate students to help control IDGE from the ground. "I still get notes from these students saying that they feel it was one of the most interesting things they did in their four years at Rensselaer," Glicksman says.

Next to the control room was a visitors' room that grew from an earlier IDGE experience during USMP-3. During that run of the experiment, "we quickly learned that you can't mix your science operations with visitors," Glicksman says, because it was too difficult to focus on both at once. So before USMP-4 flew, the team conducted a summer workshop with some 25 teachers to introduce them to microgravity science and give them materials they could use in class. At the same time, they primed them for class visits to the control center during the mission.

The visitors' room included video and audio downlinks so students could observe activities taking place aboard the shuttle, participate in hands-on demonstrations (like a miniature drop tower), and hear mini-lectures from graduate students. "It probably was the best \$25,000 we spent," Glicksman says. More than 800 elementary, junior high, and senior high school students from schools in cities around Albany, New York, learned about the value of space research from college students who were directly involved with the experiment.

Another benefit of area student involvement was extensive local news coverage. "People are very receptive" to space research, Glicksman notes. "Don't underestimate that, especially as you apply these outreach activities in areas outside of NASA centers."

Mary Musgrave: LEO Then Beyond

Mary Musgrave, associate dean of the College of Natural Sciences and Mathematics at the University of Massachusetts, also tapped into the receptiveness of the public to space research. She was the PI for the Collaborative Ukrainian Experiment (CUE) on the same shuttle mission. CUE involved 200,000 students from the United States and Ukraine in studying plant growth in space. During the mission, Payload Specialist Leonid Kadenyuk (the first Ukrainian to fly aboard a U.S. space shuttle) used a dead bee on a stick to pollinate plants. What sounds like a comedy skit is quite serious: bees and other insects are central to spreading pollen and thus fertilizing plants for subsequent seed production.

Extensive preparation and a solid set of curricular materials were important to CUE. "It works best if you can pair up with someone in the education sector who can develop the curricular materials," Musgrave explains. She had "a wonderful collaboration" with Paul Williams, of the University of Wisconsin. He developed a special dwarf stock of rapid-cycling *Brassica rapa* (also called Wisconsin Fast Plants) bred to have a 35- to 40-day life cycle so they could be used to teach biology in the classroom. Williams also wrote a 100-page teacher's guide, published by NASA, and together with educational outreach professionals at Kennedy Space Center, he conducted numerous teacher-training workshops. Students grew Williams' plants on the ground while Kadenyuk worked with them in space. To help students make connections, NASA sponsored live downlinks from the shuttle and a question-and-answer period with Kadenyuk.

Musgrave now is developing *LEO [Low Earth Orbit] Then Beyond*, a 25-page, eight-lesson teacher's guide explaining the use of plants for bioregenerative life support systems on long-duration space missions. To supplement the content of the guide, written by Musgrave, computer science graduate students are developing



Students who participate in hands-on experiments learn and understand more than those who just watch. Here, college student Pratima Rao, who was directly involved in the Isothermal Dendritic Growth Experiment, shares her insights with elementary school students during an educational outreach activity at the Rensselaer Polytechnic Institute in Troy, New York.



Ukrainian astronaut Leonid Kadenyuk worked with *Brassica rapa* plants for the Collaborative Ukrainian Experiment aboard the space shuttle on STS-87. Through live downlinks, he answered questions from students on Earth who were following the experiment.

computer-based “intelligent tutors.” The “tutors” will take the students through the plant pollination process and then check what they have learned. The Massachusetts Space Grant Consortium is funding her project in part. “These space grant consortia are good sources of small amounts of money for education outreach,” says Musgrave.

LEO Then Beyond ties in with International Space Station Mission 8A, scheduled for April 2002. Part of the payload for the mission will be the Biomass Production System, or BPS. This system provides advanced environmental control for growing and maintaining plants in space. One of its four growth chambers will be allocated to Fast Plants, which students on Earth will monitor via downlinked video. “Students will build their own versions of the growth chambers from one-gallon milk containers and grow the plants on the same schedule,” Musgrave says. Teacher workshops started in the fall of 2001. “Although the curriculum culminates with the ISS,” she continues, “it’s intended to teach about the importance of plants in space, why we experiment in microgravity, and the science behind bioregenerative life support.” The project’s industrial partners are Orbital Technologies Corporation (BPS’s builder) and Bioshelters Inc.

Aloke Chatterjee: Mentoring Students

Also helping students look beyond Earth orbit is Aloke Chatterjee, of Lawrence Berkeley National Laboratory. Chatterjee, a senior staff scientist and principal investigator in materials science, is conducting theoretical modeling of DNA damage and cellular responses during long-term space missions such as human flight to Mars. Chatterjee’s educational outreach has included mentoring summer research assistants and graduate students.

For the past 10 years he has had two students, usually minorities, from high school or college working with him each year as summer research assistants. Chatterjee noted that one difficulty in managing such a program may be the reluctance of mentors to take on the safety and health responsibilities that come with

nonprofessionals working in radiation-related work. Still, for those who get involved, “the feedback from them has always been good,” Chatterjee says.

Reaching Beyond the Classroom

For these investigators, outreach also goes beyond the classroom. Since USMP-4 was completed in December 1997, Glicksman, a fellow of the American Society for Materials (ASM) International, has visited about three ASM chapters per year, in Michigan, Pennsylvania, and New York. Each visit draws about 30 to 50 professionals, plus college and high school students. “I use the professional video that NASA made about the IDGE — it’s excellent — and lightly touch on some key spaceflight results in terms that nonexperts can appreciate,” Glicksman says. “It always goes over well, and it’s an eye-opener for people who never paid much attention to NASA missions.”

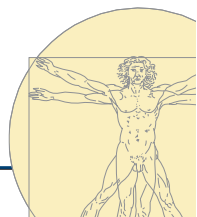
During STS-87, Musgrave was invited to give presentations to church and civic groups, government employee training sessions, and retiree programs, and to do television and radio news spots for broadcast in the United States and in Ukraine. One nursing home even used the shuttle-linked activity as recreational therapy for its residents. Chatterjee and his team frequently give talks at schools and civic clubs. Chatterjee usually starts by asking the audience if they think their tax dollars are well-spent in space. After talking about his work, he repeats the question, and gets “a lot of converts,” he says.

Perhaps Penny Terpening sums up the impact of these types of activities. The eighth-grade teacher from Berne, New York, who participated in the IDGE educational outreach project, says, “My biggest thrill there was I was trained for radio and was able to listen in on all sorts of things at the onsite communications center at [Rensselaer]. We were able to bring students over to watch some great real-time crystal growth directly from the shuttle’s downlink! . . . Too much science is taught from history when so much is happening right now!”

OBPR salutes the three featured PIs who have taken the initiative to reach out to students and the public. It is impossible to measure how far their reach has extended or to know the impact their projects may have on career choices of those involved. One thing is certain, though: they have provided effective models of how to bring their research into classrooms and to the general public.

Bonnie McClain and Dave Dooling

For more information on IDGE, go to <http://www.rpi.edu/locker/56/000756/> on the World Wide Web. For more information on Fast Plants, visit the web site at <http://fastplants.cals.wisc.edu/guide/makefp.html>. To read more about CUE, see <http://www.jsc.nasa.gov/pao/media/rel/1997/H97-270.html>. To find out more about *LEO Then Beyond*, see <http://www.cs.umass.edu/~pxhudson/nasa/main.html>. For more information on the NASA Specialized Center of Research and Training in Radiation Health, visit <http://www.lbl.gov/lifesciences/NSCORT/>.



RESEARCH OPPORTUNITIES

http://research.hq.nasa.gov/code_u/code_u.cfm

Proposals Selected in Advanced Human Support Technologies

NASA has selected 10 researchers to receive grants for the development of advanced technologies needed to produce food, recycle water and air, and monitor spacecraft environments for long-term human exploration of space. The grants total approximately \$5.4 million over a three-year period and will fund research on monitoring spacecraft habitats, plant growth in space, and water processing technology. A total of 50 research proposals were received in response to the research announcement of opportunities in advanced human support technologies. For a list of selected principal investigators, institutions, and research titles by state, visit http://spaceresearch.nasa.gov/general_info/OBPR-01-203.html on the World Wide Web (WWW).

Researchers Selected to Develop Health-Monitoring Sensors

NASA and the National Cancer Institute (NCI) received 53 proposals in response to their joint announcement soliciting research on the development of biomedical technologies to detect, diagnose, and treat diseases within the human body. Seven researchers will receive grants totaling approximately \$11 million over three years to develop and study nanoscale biomedical sensors that can detect changes at the cellular and molecular levels and can relay information regarding detected irregularities to a device outside of the body. For additional information on the NASA/NCI collaboration, visit the organizations' joint web site at <http://NASA-NCI.arc.nasa.gov>.

New Research Funded in Microgravity Fluid Physics

Thirty-five researchers have been selected by NASA to receive grants totaling approximately \$14.4 million over four years to use microgravity environments to study fundamental physical and chemical processes associated with spaceflight. The grants will support both ground-based and flight research focusing on microgravity fluid physics,

and scientists will use a variety of NASA's microgravity research facilities, including drop towers and tubes, parabolic-flight aircraft, and sounding rockets, with the goal of developing experiments for flight on the space shuttle and the International Space Station. A total of 209 proposals were received in response to the research announcement. For a list of selected principal investigators, with their institutions and project titles, visit http://spaceresearch.nasa.gov/general_info/OBPR-01-229.html on the WWW

TECHNICAL MEETINGS

2002 American Physical Society April Meeting

April 20–23, 2002

Albuquerque, New Mexico

<http://www.aps.org/meet/APR02/>

Members of the astrophysics, nuclear physics, particles and fields, physics of beams, and plasma physics divisions of the American Physical Society will deliver approximately 45 invited sessions, more than 100 contributed sessions, and a number of poster sessions at the society's annual meeting. This year, the meeting will be held in conjunction with the High Energy Astrophysics Division of the American Astronomical Society. Plenary talks given during the meeting include "High-Energy-Density Physics With Applications to Astrophysics," "The Cosmological Constant and Fundamental Physics," "High-Resolution X-Ray Studies of Globular Clusters," "Universal Scaling Laws in Biology," "Solving the Solar Neutrino Problem," and "Medium-Size Black Holes."

2002 Applied Computation Research Society Joint International Conference on Computational Nanoscience and Nanotechnology and Modeling and Simulation of Microsystems

April 22–25, 2002

San Juan, Puerto Rico

<http://www.cr.org/ICC2002/index.html>

This joint symposium will bring together the research of scientists from various areas in the simulation community who are working in micro- and nanotechnology. The conference

on computational modeling will provide a forum for the interdisciplinary blending of computational efforts that are founded on inherently similar atomistic modeling approaches but are applied to the traditionally distinct disciplines of biology, chemistry, physics, and materials science, while the conference on modeling and simulation of microsystems will provide a forum for the interdisciplinary blending of computational efforts in the microelectronics and microelectromechanical systems disciplines. Combining these two areas will enable simulation researchers to keep up with advances in applied computation research, regardless of the specific application of that research. The main topic areas to be covered in the symposium include computational biology, computational chemistry, and computational materials research. A sampling of topics to be covered includes molecular modeling, protein engineering, structural biology, bioinformatics and computational genomics, polymers and colloids, solid-state and surface chemistry, kinetics and collision dynamics, molecular electronic structure, alloys and nanostructures, nanofluidics, radiation effects in solids and cluster impact phenomena, glasses and ceramics, and large-scale simulations.

2002 NASA / Jet Propulsion Laboratory Workshop for Fundamental Physics in Space

May 9–11, 2002

Dana Point, California

<http://funphysics.jpl.nasa.gov/conference-02>

This annual workshop provides the opportunity for fundamental physics investigators to report on the progress of their various research projects and to share ideas for possible future research. Fundamental physics is a discipline of the Physical Sciences Division of the Office of Biological and Physical Research at NASA. Many of the eight Nobel laureates who take part in this research, including Wolfgang Ketterle, of the Massachusetts Institute of Technology, have been invited to attend the workshop. Topics to be discussed include laser-cooled atomic physics, gravitation and relativity physics, low-temperature condensed matter physics, and biological physics. In addition, program managers from NASA headquarters

and the Jet Propulsion Laboratory will take this opportunity to update their researchers on the “state of the discipline.”

2002 International Space Symposium

September 10–13, 2002

Toulouse, France

<http://database.spacefoundation.org/iss02/>

The U.S. Space Foundation and the French Space Agency will jointly hold the International Space Symposium, which will take place in Europe for the first time. The theme of this symposium is “Where Space Means Business.” The symposium will cover a diverse range of topics of interest to the global space industry: telecommunications, commercial remote sensing, launch vehicles, commercial satellite and ground station operations, “Internet in the sky,” and commercial solutions for government space requirements. The symposium will bring together industry executives, heads of agencies, financiers, managers, underwriters, customers, and regulators of the global space community.

PROGRAM RESOURCES

General Site

Office of Biological and Physical Research (OBPR)

<http://spaceresearch.nasa.gov>

- Latest Biological and Physical Research News
- Research on the International Space Station
- Articles on Research Activities
- Space Commercialization
- Educational Resources

Descriptions of Funded Research Projects

Science Program Projects

<http://research.hq.nasa.gov/taskbook.cfm>

Commercial Projects (also includes a description of the Commercial Space Center Program and other information)
<http://cscsourcebook.nasa.gov>

Space Life Sciences Research Resources

(for literature searches)

<http://spaceline.usuhs.mil/home/newsearch.html>

Human Physiology Research and the ISS *continued from page 11*

In ground-based research using a tissue culture model of the endothelial transport barrier, he has shown that a sudden increase in vascular pressure, which occurs in the face in microgravity, induces an early adaptive response. The endothelial layer’s resistance to the flow of water from the blood into the tissue space increases for about an hour after the pressure increases. This natural control mechanism tends to limit facial swelling. The ground-based experiments further demonstrate that after an hour of altered pressure, the resistance begins to drop substantially, leading to a condition in which there is excessive leakage of fluid from the blood to the tissue. This loss of control of transvascular transport exacerbates facial swelling.

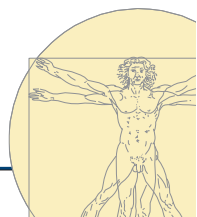
Tarbell is studying the biomolecular mechanisms that mediate the response of the endothelial transport barrier to changes in pressure. His group has found that the loss of resistance to fluid transport from blood to tissue can be blocked completely by inhibiting the formation of nitric oxide (NO) using pharmacologic agents. Findings in Tarbell’s research related to NO tie in to studies by other OBPR scientists in biomedicine and fundamental space biology who are studying how NO affects other fluid-related conditions experienced by astronauts such as bone blood flow, orthostatic intolerance (lightheadedness upon standing or sitting up), cardiac atrophy, and circadian rhythms (natural sleep patterns).

Tarbell also has found that the loss of resistance can be reversed by elevating intracellular levels of cAMP (cyclic adenosine monophosphate), a signaling molecule that affects the hydraulic conductivity of endothelial cells. As a consequence, fluid volume shifts, affecting astronauts. Tarbell says, “The results suggest a variety of possible approaches for pharmacologic intervention to regulate hydraulic activity of endothelial cells in microgravity,” thereby reducing the degree of “Moon face” and other fluid-related conditions experienced by astronauts.

On Earth, Tarbell’s research findings could provide insight into the importance of maintaining normal tissue homeostasis and knowledge about how its breakdown becomes critical in various diseases. These include atherosclerosis, a degenerative disease of arteries that underlies heart attacks and strokes; diabetic retinopathy, leakage of albumin into the retina; and when tissue is inflamed, the transvascular transport that leads to tissue edema (swelling).

Julie Moberly, with research contributions from Julie K. Poudrier and Carolyn Carter Snare

For more information on Tarbell’s research, see Tarbell, J. M., Demaio, L., & Zaw, M. M. (1999). Effect of pressure on hydraulic conductivity of endothelial monolayers: The role of endothelial cleft shear stress. *Journal of Applied Physiology*, 87, 261-268. You can also visit <http://fenske.che.psu.edu/Faculty/Tarbell/BTDL/rsch.html> on the World Wide Web (WWW). For more information on Bateman’s research, see Bateman, I. A., Dunstan, C. R., Ferguson, V. L., Lacey, D. L., Ayers, R. A., Simske, S. J. (2000). Osteoprotegerin mitigates tail suspension-induced osteopenia. *Bone*, 26, 443-449 and Bateman, I. A., Dunstan, C. R., Ferguson, V. L., Lacey, D. L., Ayers, R. A., Simske, S. J. (2001). Osteoprotegerin ameliorates sciatic nerve crush induced bone loss. *Journal of Orthopaedic Research*, 19, 518-523. More information on BioServe Research, including Bateman’s research on bone growth, is available at <http://www.colorado.edu/engineering/BioServe/research.html> on the WWW. For more information on Baldwin’s research, see Adams, G. R., McCue, S. A., Bodell, P. W., Zeng, M., and Baldwin, K. M. (2000). The effects of spaceflight on rat hindlimb development I: Muscle mass and IGF-1 expression. *Journal of Applied Physiology*, 88, 894-903 and Adams, G., Haddad, F., McCue, S. A., Bodell, P. W., Zeng, M., Qin, L., Qin, A. X., and Baldwin, K. M. (2000). The effects of spaceflight and thyroid deficiency on rat hindlimb development II: Expression of myosin heavy chain isoforms. *Journal of Applied Physiology*, 88, 904-916. For more information on research conducted by Hagan and other scientists at the Exercise Physiology Laboratory at Johnson Space Center, visit the laboratory’s web site at <http://www.jsc.nasa.gov/sa/sd/sd3/exl/>.



The ISS — The Most Unique Laboratory in the Universe *continued from page 13*

and products. Three experiments are also set up to study macromolecular crystal growth. A crystal growth facility on the station allows researchers to grow better-ordered protein crystals than can be grown on Earth, enabling scientists to better understand the molecular structure of biochemically significant proteins, and ultimately, their functions. In addition, an experiment in materials science will help shed new light on the factors that control alloy solidification.

Other experiments look at problems encountered in human space travel. Fire safety is a major concern on the ISS, and one experiment studies the mechanisms of smoldering combustion. Radiation is also a major hazard, and the Prototype Synchrotron Radiation Detector is being tested on the shuttle for possible use on the ISS. Two acceleration measurement systems being tested will record changes in the microgravity acceleration on the station. The Cellular Biotechnology Operations Support System is the first on-station hardware that is dedicated to cultivating living tissue cells, which will be beneficial because tissues grown in microgravity more closely resemble in-vivo tissues than those grown on Earth. Still more experiments are in the preparation stages and will be flown on future expeditions.

OBPR's **Research Integration Division** promotes commercialism in space by

creating partnerships between NASA and the business community. NASA hopes to demonstrate the commercial potential of space by showing the advantages of microgravity research for industry. To that end, commercial space centers (CSCs), which support a diverse range of commercial product research and development efforts in fields including agriculture, combustion, electronic devices, biotechnology, and materials processing, are a key program area for the division. The CSCs are using knowledge gained from shuttle flights to develop cost-effective and efficient flight hardware for extended-duration commercial research on the ISS.

Several CSC payloads have successfully operated on the ISS: Commercial Protein Crystal Growth for biomedical drug development and protein crystal growth research, and Advanced Astroculture™ for agriculture research in microgravity using a closed-environment system to develop the capability for seed-to-seed plant life cycles and genetic engineering research in microgravity. The STS-108 mission transported the Advanced Astroculture project to the ISS for a repeat research mission along with a new payload, the Zeolite Crystal Growth (ZCG) furnace. Subsequent missions will bring zeolite crystal samples to the station for microgravity processing in the furnace.

The potential for ZCG materials processing research to develop larger and better-ordered zeolite crystals has significant refining, biomedical, and electronic device applications.

In addition to these payloads planned for the near future, other biotechnology and materials processing hardware elements are in development, either as next-generation versions of prior, shuttle-originated payloads or as a means of providing new flight hardware capabilities for commercial research on the ISS.

The ISS is indeed the world's most unique laboratory. A major stumbling block to microgravity research — limited experiment time — has been removed. No longer will experiments have to be conducted over only a few days on a space shuttle mission. Now scientists can plan on having weeks, months, and even years to allow their particular studies to evolve. With projects from the United States as well as from many other countries in progress at the station, one can see the beginnings of a new age of scientific research in orbit around Earth.

*Julie K. Poudrier
and Carolyn Carter Snare*

Physical Sciences *continued from page 19*

launched aboard a Russian Progress rocket on February 26, 2001. It is funded primarily by the German space agency, the DLR, and is conducted in cooperation with the High Energy Density Research Center in Moscow, Russia. Data from the experiment, the first to be performed on the ISS, are obtained through the use of video recordings of the melting process that are returned to Earth after resupply missions to the ISS. So far, some 40 hours of experiments have been run.

New Tools Foster New Discoveries

Although astronomers have long known about dusty plasmas in interstellar space, the ability to make dusty plasmas in the laboratory has proven key to making new discoveries. Early results from the ground-based and flight-based experiments are stimulating the development of new theories

to describe the melting process in dusty plasmas and the subsequent phase change that takes place in the material. "In fact," says Goree, "the field of dusty plasmas has been experiencing a very rapid growth in publications in the past 10 years."

Dusty plasma research may also get a big boost from a long-term facility that's being designed for conducting dusty plasma experiments aboard the space station. The International Microgravity Plasma Facility has passed the feasibility study, which assesses many practical details of the design, operation, and use of the facility given certain space station capabilities and restrictions. The project is led by the DLR, which is seeking partners to share in both the resources required to build the facility and in the use of the facility for research. "The facility would have many of the same kinds of components built for PKE, but

unlike PKE, it is designed to be reusable and adaptable," Goree explains.

Goree is looking forward to the opportunities opened up for him by the ISS. He sums up the significance of new tools and facilities to conduct research and the excitement of discovery: "When you have a new kind of experimental tool, it allows you to make new kinds of experiments or observations that were previously impossible to do. That stimulates a whole scientific community to grow. You get lots of new kinds of phenomena that were previously unobserved. It all just snowballs."

Jacqueline Freeman-Hathaway

For more information on Goree's research, visit <http://www.microgravity.net> and <http://dusty.physics.uiowa.edu/~goree>. Results of research on sound wave propagation in two-dimensional dusty plasma crystals were published in Melzer, A., Nunomura, S., Samsonov, D., Ma, Z. W., and Goree, J., (2000). Laser-excited mach cones in a dusty plasma crystal. *Physical Review E*, 62, 4162-4176.

Profile: Alice Gast

Alice Gast envisions a future for science in which disciplines have flexible borders and researchers collaborate across those borders.

The idea of individual scientists making startling discoveries while working in isolation at a bench is a romantic one. Although notable achievements are still made by individuals in their respective fields, scientists are recognizing a growing benefit to collaborating across disciplines to enhance their research. As they have delved deeper into the mysteries of the world around them, researchers have found that the boundaries of their individual disciplines are blurred. One example of such a sea change is in the area of biotechnology, where developing a miniaturized robot for medical purposes might require knowledge of the fields of medicine, engineering, and physics, among others.

Does this mean that today's young researchers must learn to be masters of all disciplines? No. According to NASA Principal Investigator Alice Gast, who also serves as the new vice president of research, associate provost, and professor of engineering at the Massachusetts Institute of Technology (MIT), the key is to foster among students working interdisciplinary relationships and peer-to-peer learning experiences that they can carry over into their professional lives.

Gast, a chemical engineer who received her undergraduate degree from the University of Southern California and her doctorate from Princeton University, is quite familiar with cross-disciplinary research. Some of Gast's research focuses on interfacial phenomena, an area of interest to biological and biomedical researchers as well as to chemical engineers.

Gast became interested in working with NASA when she attended conferences where she met researchers from the complex fluids and fluid physics groups at Lewis Research Center (now Glenn Research Center). After discovering common interests with the NASA researchers and discussing their various research projects, Gast decided to submit a proposal to NASA requesting funding for her research at Stanford University on the properties of magnetic colloids.

In addition to her research and teaching duties at Stanford, Gast was also instrumental in the development of Stanford's Clark Center for Biomedical Engineering and Sciences. The Clark Center is the centerpiece of Stanford's Bio-X program, which, remarks Gast, "will bring people from the medical, engineering, and



credit: Marc Fernigier

science [fields] together to work on areas where their expertise overlaps but [where] they're truly working at the boundaries of their fields." Allowing people from different fields to more easily interact will enable researchers in one field to benefit from the different approaches that researchers from another field can bring to a specific problem.

Gast hopes to continue to promote such interdisciplinary collaboration at MIT. "I'd like to try to help push the boundaries of the way we have laboratory spaces and interactions and push down the barriers between departments and schools to try to foster productive research environments," she says.

Gast recognizes the importance of encouraging the interdisciplinary interactions that succeed. Says Gast, "The ones that really work come from the scientists figuring out that they need each other and want to work with each other more than [from] a funding structure that forces collaboration."

Another part of Gast's interdisciplinary philosophy is that she believes institutions funding research need to make sure that exciting, emerging areas of research are not lost simply because they do not fall into current research categories. "The thing you really want to do," she says, "is make sure you're not discouraging the people who are at the edges or boundaries of what your normal program is. You don't want a proposal to arrive and not be able to figure out which group should fund it.

"I think there's some concern in scientific communities," she continues,

"that if you're on the edge of your discipline you will fall out of it and you won't really fall into another one. Some government agencies are not good at those gray edges. NASA, however, has been very proactive in trying to foster new initiatives and new areas of research."

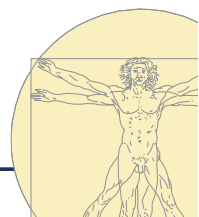
As for young principal investigators, Gast suggests that they learn more about an agency before submitting a proposal. "I think it's useful to contact a grant monitor or program manager to touch base with them about what you're thinking and whether they think it fits into their program," she says.

Gast notes that there has been "some great synergy" in her own past collaborations, "especially for me bringing together the synthetic chemists and the people who actually make things — the biochemists and chemists with the physical scientists and engineers — because we think about problems differently and we bring different capabilities to the table, and then we can make new things and understand them and look at them in new ways, so it's quite fruitful."

Gast's enthusiasm for the benefits of interdisciplinary collaboration and learning from peers will follow her to her new position at MIT, where she hopes to have the same type of success she's had with NASA and Stanford's Bio-X program. Her vision of the future of science as a field with more flexible borders may inspire the next generation of scientists, leading to unimaginable discoveries. It is a future worth striving for.

Julie K. Poudrier

If you would like to reach Alice Gast to discuss her research, you may e-mail her at gast@mit.edu.



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